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     (FILE 'HOME' ENTERED AT 17:22:36 ON 12 JUN 2007)

     FILE 'CAPLUS, MEDLINE' ENTERED AT 17:23:07 ON 12 JUN 2007
L1             2 S HYALURONIC ACID? (P) BENZYL ESTER? (P) TUMOR?
L2             2 S HYALURONIC ACID? (P) BENZYL? (P) TUMOR?
L3            28 S HYALURONIC ACID? (P) ESTER? (P) TUMOR?
L4            26 S L3 NOT L2
L5             7 S L4 AND PRIMAR?
L6             0 S L4 AND CROSSLINKL?
L7             0 S L4 AND CROSSLINK?
L8             0 S L4 AND CROSS-LINK?
L9             0 S L4 AND CROSSLINK?
L10            0 S L4 AND PHENYMETHYL
L11            0 S L4 AND PHENY METHYL
L12           19 S L4 NOT L5
L13            1 S L12 AND SECOND?
L14           18 S L12 NOT L13
L15            0 S CROSSLINKED HYALURONIC ACID? (P) BENZYL? (P) TUMOR?
L16            0 S CROSS-LINKED HYALURONIC ACID? (P) BENZYL? (P) TUMOR?
L17            0 S CROSS-LINKED HYALURONIC ACID? (P) ESTER? (P) PRIMARY TUMOR?
L18            0 S CROSSLINKED HYALURONIC ACID? (P) ESTER? (P) TUMOR?
L19            1 S CROSSLINKED HYALURONIC ACID? (P) TUMOR?
L20            0 S CROSSLINKED HYALURONIC ACID? (P) CANCER?
L21            1 S ?CROSSLINKED HYALURONIC ACID? (P) TUMOR?
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L23            0 S ?CROSSLINKED HYALURONIC ACID? (P) ?CANCER?
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L32            2 S L31 AND ESTER?
L33           10 S L31 NOT L32
L34            0 S HYALURONIC ACID? (P) ?TUMOR? (P) ?METHYLPHENYL?
L35            3 S HYALURONIC ACID? (P) ?TUMOR? (P) ?PHENYLMETHYL?
L36           76 S HYALURONIC ACID? (P) ?TUMOR? (P) ?ESTER?
L37            6 S L36 AND ANGIOGENESIS
L38            2 S HYALURONAN? ?BENZYL? ?ESTER? (P) ?TUMOR? (P) ?ESTER?
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L42            2 S L41 NOT L39
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L45            1 S ?HYAFF? (P) ?CANCER?
L46           15 S ?CROSSLINK? (P) HYALURONIC ACID? (P) ?TUMOR?
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     (FILE 'HOME' ENTERED AT 17:22:36 ON 12 JUN 2007)

     FILE 'CAPLUS, MEDLINE' ENTERED AT 17:23:07 ON 12 JUN 2007
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L3            28 S HYALURONIC ACID? (P) ESTER? (P) TUMOR?
L4            26 S L3 NOT L2
L5             7 S L4 AND PRIMAR?
L6             0 S L4 AND CROSSLINKL?
L7             0 S L4 AND CROSSLINK?
L8             0 S L4 AND CROSS-LINK?
L9             0 S L4 AND CROSSLINK?
L10            0 S L4 AND PHENYMETHYL
L11            0 S L4 AND PHENY METHYL
L12           19 S L4 NOT L5
L13            1 S L12 AND SECOND?
L14           18 S L12 NOT L13
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L23            0 S ?CROSSLINKED HYALURONIC ACID? (P) ?CANCER?
L24            0 S ?CROSSLINKED HYALURONIC ACID? (P) ANGIOGENESIS  (P) INHIBIT?
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L27            0 S ?CROSSLINK? HYALURONIC ACID? (P) ?CANCER?
L28            0 S ?CROSSLINK? HYALURONATE? (P) ?TUMOR?
L29            3 S ?CROSSLINK? (P) HYALURONATE? (P) ?TUMOR?
L30         1303 S HYALURONIC ACID? (P) ?TUMOR?
L31           12 S HYALURONIC ACID? (P) ?TUMOR? (P) ?BENZYL?
L32            2 S L31 AND ESTER?
L33           10 S L31 NOT L32
L34            0 S HYALURONIC ACID? (P) ?TUMOR? (P) ?METHYLPHENYL?
L35            3 S HYALURONIC ACID? (P) ?TUMOR? (P) ?PHENYLMETHYL?
L36           76 S HYALURONIC ACID? (P) ?TUMOR? (P) ?ESTER?
L37            6 S L36 AND ANGIOGENESIS
L38            2 S HYALURONAN? ?BENZYL? ?ESTER? (P) ?TUMOR? (P) ?ESTER?
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L41            4 S HYAFF? (P) ?TUMOR?
L42            2 S L41 NOT L39
L43            1 S HYAFF? (P) ?CANCER?
L44            4 S ?HYAFF? (P) ?TUMOR?
L45            1 S ?HYAFF? (P) ?CANCER?
L46           15 S ?CROSSLINK? (P) HYALURONIC ACID? (P) ?TUMOR?
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L1 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:694981 CAPLUS
DOCUMENT NUMBER: 143:482971
TITLE: Implantation of preadipocyte-loaded hyaluronic acid-based scaffolds into nude mice to evaluate potential for soft tissue engineering
AUTHOR(S): Hemmrich, Karsten; von Heimburg, Dennis; Rendchen, Raoul; Di Bartolo, Chiara; Milella, Eva; Pallua, Norbert
CORPORATE SOURCE: Department of Plastic Surgery and Hand Surgery, University Hospital of the Aachen University of Technology, Aachen, D-52057, Germany
SOURCE: Biomaterials (2005), 26(34), 7025-7037
CODEN: BIMADU; ISSN: 0142-9612
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The reconstruction of soft tissue defects following extensive deep burns or tumor resections remains an unresolved problem in plastic and reconstructive surgery since adequate implant materials are still not available. Preadipocytes, immature precursor cells found between mature adipocytes in adipose tissue, are a potential material for soft tissue engineering since they can proliferate and differentiate into adipose tissue after transplantation. In previous studies, the authors identified hyaluronan benzyl ester (HYAFF-11) sponges to be promising carrier matrixes. This study now evaluates, in vitro and in vivo, a new sponge architecture with pores of 400 μm either made of plain HYAFF-11 or HYAFF-11 coated with the extracellular matrix glycosaminoglycan hyaluronic acid. Human preadipocytes were isolated, seeded onto carriers and implanted into nude athymic mice. Explants harvested after 3, 8, and 12 wk were examined for macroscopical appearance, thickness, weight, pore structure, histol., and immunohistochem. Compared to previous studies, the authors found better penetration of cells into both types of scaffolds, with more extensive formation of new vessels throughout the construct but with only minor adipose tissue. The authors' encouraging results contribute towards a better seeded and vascularized scaffold but also show that the enhancement of adipogenic conversion of preadipocytes remains a major task for further in vivo expts.
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L1 ANSWER 2 OF 2 MEDLINE on STN
ACCESSION NUMBER: 2005400405 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15964623
TITLE: Implantation of preadipocyte-loaded hyaluronic acid-based scaffolds into nude mice to evaluate potential for soft tissue engineering.
AUTHOR: Hemmrich Karsten; von Heimburg Dennis; Rendchen Raoul; Di Bartolo Chiara; Milella Eva; Pallua Norbert
CORPORATE SOURCE: Department of Plastic Surgery and Hand Surgery, Burn Centre, University Hospital of the Aachen University of Technology, Germany.
SOURCE: Biomaterials, (2005 Dec) Vol. 26, No. 34, pp. 7025-37.
Journal code: 8100316. ISSN: 0142-9612.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (EVALUATION STUDIES)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200512
ENTRY DATE: Entered STN: 3 Aug 2005

Last Updated on STN: 15 Dec 2005
Entered Medline: 7 Dec 2005

AB The reconstruction of soft tissue defects following extensive deep burns or tumor resections remains an unresolved problem in plastic and reconstructive surgery since adequate implant materials are still not available. Preadipocytes, immature precursor cells found between mature adipocytes in adipose tissue, are a potential material for soft tissue engineering since they can proliferate and differentiate into adipose tissue after transplantation. In previous studies, we identified hyaluronan benzyl ester (HYAFF 11) sponges to be promising carrier matrices. This study now evaluates, in vitro and in vivo, a new sponge architecture with pores of 400 microm either made of plain HYAFF 11 or HYAFF 11 coated with the extracellular matrix glycosaminoglycan hyaluronic acid. Human preadipocytes were isolated, seeded onto carriers and implanted into nude athymic mice. Explants harvested after 3, 8, and 12 weeks were examined for macroscopical appearance, thickness, weight, pore structure, histology, and immunohistochemistry. Compared to previous studies, we found better penetration of cells into both types of scaffolds, with more extensive formation of new vessels throughout the construct but with only minor adipose tissue. Our encouraging results contribute towards a better seeded and vascularised scaffold but also show that the enhancement of adipogenic conversion of preadipocytes remains a major task for further in vivo experiments.

L5 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1075830 CAPLUS
DOCUMENT NUMBER: 143:360080
TITLE: Hyaluronic acid butyric esters with a low degree of substitution, procedure for their preparation, and their use in the treatment of cancer
INVENTOR(S): Coradini, Danila; Perbellini, Alberto
PATENT ASSIGNEE(S): Sintofarm S.p.A., Italy
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005092929	A1	20051006	WO 2005-IB780	20050325
WO 2005092929	A8	20060302		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1781707	A1	20070509	EP 2005-718276	20050325
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				

PRIORITY APPLN. INFO.: IT 2004-MI605 A 20040329
WO 2005-IB780 W 20050325
OTHER SOURCE(S): CASREACT 143:360080
AB The invention discloses hyaluronic acid butyric esters in which the hydroxyl groups of hyaluronic acid are partially esterified with butyric residues, characterized by a degree of substitution with butyric residues (ratio of number of butyric acid residues to disaccharide units GlcNAc-GlcUA of hyaluronic acid) being equal or below 0.1. These esters with low degree of substitution are obtained by means of a process carried out in the homogeneous phase under anhydrous conditions, wherein hyaluronic acid is used in the form of a quaternary nitrogen salt. The esters of the invention have a greater antiproliferative activity than corresponding esters with higher degree of substitution, and are particularly active against primary and metastatic tumors, where the tumors are primary of hepatic origin, or are hepatic metastases. A further aspect of the invention is represented by pharmaceutical compns., containing as active principle at least one of the esters described.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:178896 CAPLUS
DOCUMENT NUMBER: 142:384899
TITLE: Hyaluronic acid butyric esters in cancer therapy
AUTHOR(S): Speranza, Annalisa; Pellizzaro, Cinzia; Coradini, Danila
CORPORATE SOURCE: Unit of Biomolecular Determinants in Prognosis and Therapy, Experimental Department, Istituto Nazionale

per lo Studio e la Cura dei Tumori, Milan, Italy
SOURCE: Anti-Cancer Drugs (2005), 16(4), 373-379
CODEN: ANTDEV; ISSN: 0959-4973
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB In this review the authors focus on a promising novel histone deacetylase (HDAC) inhibitor (HA-But) obtained by the esterification of butyric acid (BA), the smallest HDAC inhibitor, with hyaluronic acid (HA), the main constituent of the extracellular matrix which selectively recognizes a transmembrane receptor (CD44) overexpressed in most primary cancers and associated with tumor progression. In vitro, HA-But has proved to be 10-fold more effective than BA in inhibiting the proliferation of a panel of human cancer cell lines, representative of the most common human cancers, and, similar to BA, to regulate the expression of some cell cycle-related proteins, to induce growth arrest in the G1/G0 phase of the cell cycle and to increase histone acetylation. In vivo, HA-But treatment has demonstrated a marked potency in inhibiting primary tumor growth and lung metastases formation from murine Lewis lung carcinoma (LL3) as well as liver metastases formation from intrasplenic implantation of LL3 or B16-F10 murine melanoma cells. In particular, the effect of s.c. and i.p. treatment with HA-But on liver metastases resulted, resp., in 87 and 100% metastases-free animals, and in a significant prolongation of the survival time compared to the control groups. The results suggest that the presence of the HA backbone does not interfere with the biol. activity of butyric residues and that HA-But could represent a promising cell-targetable antineoplastic agent for the treatment of primary and metastatic tumors.
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:359113 CAPLUS
DOCUMENT NUMBER: 142:85944
TITLE: Hyaluronic-acid butyric esters as promising antineoplastic agents in human lung carcinoma: A preclinical study
AUTHOR(S): Coradini, Danila; Pellizzaro, Cinzia; Abolafio, Gabriella; Bosco, Marco; Scarlata, Ignazio; Cantoni, Silvia; Stucchi, Luca; Zorzet, Sonia; Turrin, Claudia; Sava, Gianni; Perbellini, Alberto; Daidone, Maria Grazia
CORPORATE SOURCE: Unit of Biomolecular Determinants in Prognosis and Therapy, Experimental Department, Istituto Nazionale per lo Studio e la Cura dei Tumori, Milan, Neth.
SOURCE: Investigational New Drugs (2004), 22(3), 207-217
CODEN: INNDDK; ISSN: 0167-6997
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB New promising compds., derived from the esterification of hyaluronic acid with butyric acid, were investigated in vitro on a non-small cell lung carcinoma cell line (NCI-H460) and an its metastatic subclone (NCI-H460M). All new compds. exerted a dose-dependent inhibitory effect on both cell lines, which expressed CD44, the sp. surface receptor for hyaluronic acid, in a very high percentage of cells (90%). HE1, the most effective of these compds., was 10-fold more effective than sodium butyrate (NaB) in inhibiting cell proliferation. Similarly to NaB, after 24 h of treatment, HE1 affected the expression of three cell cycle-related proteins (p27kip1, p53 and p21waf1) responsible for growth arrest, indicating that the presence of the hyaluronic acid backbone does not interfere with the biol. activity. Intratumoral treatment with HE1 demonstrated a marked

efficacy on primary tumor growth and on lung metastases formation of the murine Lewis Lung Carcinoma model. Altogether, present findings suggest a possible clin. application of these novel butyric pro-drugs in primary and metastatic lung cancer.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1990:30845 CAPLUS
DOCUMENT NUMBER: 112:30845
TITLE: Effects of thyroid-stimulating hormone and phorbol ester on glycosaminoglycan synthesis in porcine thyroid epithelial cells in primary culture
AUTHOR(S): Wegrowski, J.; Bellon, G.; Haye, B.; Borel, J. P.
CORPORATE SOURCE: Lab. Biochim., Fac. Med., Reims, 51095, Fr.
SOURCE: Cell Biology International Reports (1989), 13(10), 881-90
CODEN: CBRPDS; ISSN: 0309-1651
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of TSH and of a tumor promoter (12-O-tetradecanoyl-phorbol-13-acetate) on glycosaminoglycan (GAG) synthesis were studied in porcine thyroid epithelial cells in primary culture. TSH is known to involve a cAMP mechanism and phorbol ester to act by the protein kinase C pathway. Chronic treatment of cells with TSH increased the synthesis of heparan sulfate associated with the cell layer and hyaluronic acid in the culture medium. Phorbol ester increased the radioactivity (from [3H]glucosamine and [35S]sulfate) of total GAGs in the culture medium but had no effect on GAGs associated with the cell layer. It inhibited the pos. effect of TSH on heparan sulfate synthesis. In thyroid epithelial cells, the synthesis of the GAGs associated with the cell layer and those secreted into the culture medium are evidently regulated by different intracellular mechanisms.

L5 ANSWER 5 OF 7 MEDLINE on STN

ACCESSION NUMBER: 2005115084 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15746573
TITLE: Hyaluronic acid butyric esters in cancer therapy.
AUTHOR: Speranza Annalisa; Pellizzaro Cinzia; Coradini Danila
CORPORATE SOURCE: Unit of Biomolecular Determinants in Prognosis and Therapy, Experimental Department, Istituto Nazionale per lo Studio e la Cura dei Tumori, Milan, Italy.
SOURCE: Anti-cancer drugs, (2005 Apr) Vol. 16, No. 4, pp. 373-9.
Ref: 32
Journal code: 9100823. ISSN: 0959-4973.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200507
ENTRY DATE: Entered STN: 5 Mar 2005
Last Updated on STN: 6 Jul 2005
Entered Medline: 5 Jul 2005

AB In this review we focus on a promising novel histone deacetylase (HDAC) inhibitor (HA-But) obtained by the esterification of butyric acid (BA), the smallest HDAC inhibitor, with hyaluronic acid (HA), the main constituent of the extracellular matrix which selectively recognizes a transmembrane receptor (CD44) overexpressed in most primary cancers and associated with tumor progression. In vitro, HA-But has proved to be 10-fold more effective than BA in inhibiting the proliferation of a panel of human cancer cell lines, representative of the most common human cancers, and, similar to

BA, to regulate the expression of some cell cycle-related proteins, to induce growth arrest in the G1/G0 phase of the cell cycle and to increase histone acetylation. In vivo, HA-But treatment has demonstrated a marked potency in inhibiting primary tumor growth and lung metastases formation from murine Lewis lung carcinoma (LL3) as well as liver metastases formation from intrasplenic implantation of LL3 or B16-F10 murine melanoma cells. In particular, the effect of s.c. and i.p. treatment with HA-But on liver metastases resulted, respectively, in 87 and 100% metastases-free animals, and in a significant prolongation of the survival time compared to the control groups. The results suggest that the presence of the HA backbone does not interfere with the biological activity of butyric residues and that HA-But could represent a promising cell-targetable antineoplastic agent for the treatment of primary and metastatic tumors.

L5 ANSWER 6 OF 7 MEDLINE on STN
ACCESSION NUMBER: 2004222806 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15122068
TITLE: Hyaluronic-acid butyric esters as promising antineoplastic agents in human lung carcinoma: a preclinical study.
AUTHOR: Coradini Danila; Pellizzaro Cinzia; Abolafio Gabriella; Bosco Marco; Scarlata Ignazio; Cantoni Silvia; Stucchi Luca; Zorzet Sonia; Turrin Claudia; Sava Gianni; Perbellini Alberto; Daidone Maria Grazia
CORPORATE SOURCE: Unit of Biomolecular Determinants in Prognosis and Therapy, Experimental Department, Istituto Nazionale per lo Studio e la Cura dei Tumori, Milano, Italy.. danila.coradini@istitutotumori.mi.it
SOURCE: Investigational new drugs, (2004 Aug) Vol. 22, No. 3, pp. 207-17.
Journal code: 8309330. ISSN: 0167-6997.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200411
ENTRY DATE: Entered STN: 5 May 2004
Last Updated on STN: 19 Dec 2004
Entered Medline: 22 Nov 2004

AB New promising compounds, derived from the esterification of hyaluronic acid with butyric acid, were investigated in vitro on a non-small cell lung carcinoma cell line (NCI-H460) and an its metastatic subclone (NCI-H460M). All new compounds exerted a dose-dependent inhibitory effect on both cell lines, which expressed CD44, the specific surface receptor for hyaluronic acid, in a very high percentage of cells (90%). HE1, the most effective of these compounds, was 10-fold more effective than sodium butyrate (NaB) in inhibiting cell proliferation. Similarly to NaB, after 24 hours of treatment, HE1 affected the expression of three cell cycle-related proteins (p27(kip1), p53 and p21(waf1)) responsible for growth arrest, indicating that the presence of the hyaluronic acid backbone does not interfere with the biologic activity. Intratumoral treatment with HE1 demonstrated a marked efficacy on primary tumor growth and on lung metastases formation of the murine Lewis Lung Carcinoma model. Altogether, present findings suggest a possible clinical application of these novel butyric pro-drugs in primary and metastatic lung cancer.

L5 ANSWER 7 OF 7 MEDLINE on STN
ACCESSION NUMBER: 90030452 MEDLINE
DOCUMENT NUMBER: PubMed ID: 2805078
TITLE: Effects of thyroid-stimulating hormone and phorbol ester on glycosaminoglycan synthesis in porcine thyroid epithelial

cells in primary culture.

AUTHOR: Wegrowski J; Bellon G; Haye B; Borel J P
CORPORATE SOURCE: Laboratoire de Biochimie, UA CNRS 610, Faculte de Medecine, Reims, France.

SOURCE: Cell biology international reports, (1989 Oct) Vol. 13, No. 10, pp. 881-90.
Journal code: 7708050. ISSN: 0309-1651.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198912
ENTRY DATE: Entered STN: 28 Mar 1990
Last Updated on STN: 28 Mar 1990
Entered Medline: 21 Dec 1989

AB The effects of thyroid-stimulating hormone (TSH) and a tumor promoter: 12-0-tetradecanoyl-phorbol-13-acetate on glycosaminoglycan (GAG) synthesis were studied in porcine thyroid epithelial cells in primary culture. TSH is known to involve cyclic AMP mechanism and phorbol ester to act by protein kinase C pathway. Chronic treatment of cells with TSH increased the synthesis of heparan sulphate associated with the cell layer and hyaluronic acid in the culture medium. Phorbol ester increased the radioactivity of total GAGs in the culture medium but had no effect on GAGs associated with the cell layer. It inhibited the positive effect of TSH on heparan sulphate synthesis. These results suggest that in thyroid epithelial cells the synthesis of the GAGs associated with the cell layer and those secreted into the culture medium are regulated by different intracellular mechanisms.

L13 ANSWER 1 OF 1 MEDLINE on STN

ACCESSION NUMBER: 2004364551 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15269158

TITLE: Inhibition of hepatocellular carcinomas in vitro and hepatic metastases in vivo in mice by the histone deacetylase inhibitor HA-But.

AUTHOR: Coradini Danila; Zorzet Sonia; Rossin Raffaella; Scarlata Ignazio; Pellizzaro Cinzia; Turrin Claudia; Bello Michele; Cantoni Silvia; Speranza Annalisa; Sava Gianni; Mazzi Ulderico; Perbellini Alberto

CORPORATE SOURCE: Unit of Biomolecular Determinants in Prognosis and Therapy, Experimental Department, Istituto Nazionale per lo Studio e la Cura dei Tumori, Milan.. Danila.Coradini@istitutotumori.mi.it

SOURCE: Clinical cancer research : an official journal of the American Association for Cancer Research, (2004 Jul 15) Vol. 10, No. 14, pp. 4822-30.
Journal code: 9502500. ISSN: 1078-0432.

PUB. COUNTRY: United States

DOCUMENT TYPE: (COMPARATIVE STUDY)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200501

ENTRY DATE: Entered STN: 23 Jul 2004
Last Updated on STN: 20 Jan 2005
Entered Medline: 19 Jan 2005

AB PURPOSE: The purpose is to evaluate the CD44-mediated cellular targeting of HA-But, a hyaluronic acid esterified with butyric acid (But) residues, to hepatocellular carcinoma cell lines in vitro and to hepatic tumor metastases in vivo. EXPERIMENTAL DESIGN: In vitro, the CD44-dependent cytotoxicity in two human hepatocellular carcinoma cell lines (HepB3 and HepG2) with high and low CD44 expression was investigated; in vivo, the effect on liver metastases originating from intrasplenic implants of Lewis lung carcinoma (LL3) or B16-F10 melanoma in mice was compared with the pharmacokinetics of organ and tissue distribution using different routes of administration. RESULTS: HepB3 and HepG2 cell lines showed different expression of CD44 (78 and 18%, respectively), which resulted in a CD44-dependent HA-But inhibitory effect as demonstrated also by the uptake analysis performed using radiolabeled HA-But ((99m)Tc-HA-But). Pharmacokinetic studies showed different rates of (99m)Tc-HA-But distribution according to the route of administration (i.v., i.p., or s.c.): very fast (a few minutes) after i.v. treatment, with substantial accumulation in the liver and spleen; relatively slow after i.p. or s.c. treatment, with marked persistence of the drug at the site of injection. The effect of s.c. and i.p. treatment with HA-But on liver metastases originating from intrasplenic implants of LL3 carcinoma or B16-F10 melanoma (both CD44-positive: 68 and 87%, respectively), resulted in 87 and 100% metastases-free animals, respectively (regardless of the route of administration), and a significant prolongation of the life expectancy compared with control groups. CONCLUSIONS: HA-But tends to concentrate in the liver and spleen and appears to be a promising new drug for the treatment of intrahepatic tumor lesions.

L14 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:253139 CAPLUS
DOCUMENT NUMBER: 118:253139
TITLE: CD44 antibody stimulates adhesion of peripheral blood T cells to keratinocytes through the leukocyte function-associated antigen-1/intercellular adhesion molecule-1 pathway
AUTHOR(S): Bruynzeel, Ineke; Koopman, Gerrit; van der Raaij, Liesbeth M. H.; Pals, Steven T.; Willemze, Rein
CORPORATE SOURCE: Dep. Dermatol., Free Univ. Hosp., Amsterdam, 1081 HV, Neth.
SOURCE: Journal of Investigative Dermatology (1993), 100(4), 424-8
CODEN: JIDEAE; ISSN: 0022-202X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Close contact between T lymphocytes and keratinocytes is an important feature of many inflammatory skin diseases. iN vitro studies showed that simulation of keratinocytes with interferon-γ or tumor necrosis factor-α and of T cells with phorbol esters results in a leukocyte function-associated antigen (LFA)-1/intercellular adhesion mol. (ICAM)-1-mediated adhesion. The present study was performed to investigate the role of the CD44 mol. in keratinocyte/T-cell binding. The CD44 class of lymphocyte adhesion receptors is involved in lymphocyte binding to high endothelial venules and to extracellular matrix compds. and is therefore important in lymphocyte recirculation and homing. Moreover, CD44 can act as a co-stimulating signal in T-cell activation and promotes homotypic adhesion of in vitro cultured CD3-stimulated T cells. Using a cell adhesion assay a sixfold increase in T-cell/keratinocyte adhesion was found after pre-incubating the T cells with anti-CD44. This increased adhesion was found to require an intact cytoskeleton, to be energy and magnesium dependent, and could be completely inhibited by anti-LFA-1 and anti-ICAM-1. Pretreatment of T cells with hyaluronic acid, a ligand for CD44 and an extracellular matrix compound in the dermis and epidermis, did not affect T-cell/keratinocyte adhesion.

L14 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1974:460434 CAPLUS
DOCUMENT NUMBER: 81:60434
TITLE: Colloidal iron used at pH values lower than 1 as electron stain for surface proteins
AUTHOR(S): Blanquet, Pierre R.; Loiez, Annie
CORPORATE SOURCE: Inst. Rech. Cancer, Inst. Natl. Sante Rech. Med., Lille, Fr.
SOURCE: Journal of Histochemistry and Cytochemistry (1974), 22(5), 368-77
CODEN: JHCYAS; ISSN: 0022-1554
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cl- at pH <1 changed the conventional pos. charged ferric hydroxide colloid to a neg. form. This neg. colloid can be used as a new cytochem. method at the electron microscopic level to visualize, with relative specificity, pos. ionized groups such as the basic amino groups of protein side chains in the outer and inner hydrophilic leaflets of the cell surface membrane. The effects of HCl on the stability, charge and selective affinity of the colloidal ferric hydroxide were studied. The charge was tested electrophoretically. The stability was controlled by measuring the turbidity. The affinity was determined by applying colloid to gelled agarose sections containing hyaluronic acid, poly(vinyl sulfate) or polylysine. Affinity was also determined by applying the colloid to free tumor cells previously submitted to various types of chemical and enzymic treatments (esterification,

acetylation, periodic acid-hydroxylamine method; neuraminidase, phospholipase C, hyaluronidase) and to isolated rat liver surface membranes pretreated by lipid extraction or incubated with phospholipase C.

L14 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1959:84856 CAPLUS
DOCUMENT NUMBER: 53:84856
ORIGINAL REFERENCE NO.: 53:15319g-h
TITLE: Histochemical study of mucopolysaccharides in mixed tumors of salivary glands
AUTHOR(S): D'Ancona, Siliva; Rotelli, Luigi
CORPORATE SOURCE: Univ. Milan
SOURCE: Rivista di Istochimica Normale e Patologica (1958), 4, 249-68
CODEN: RINPAF; ISSN: 0485-2400
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB The examination of 18 tumors (7 myxoid, 6 predominantly cellular, 4 extremely cellular, according to Foote and Fraxell's classification) by several techniques for mucopolysaccharide detection showed the presence of acid mucopolysaccharides of connective origin (hyaluronic acid) in the hyaline areas, and of highly polymeric mucpolysaccharides with various degrees of esterification in the myxoid areas. The origin of the myxoid stroma is discussed.

L14 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1956:41493 CAPLUS
DOCUMENT NUMBER: 50:41493
ORIGINAL REFERENCE NO.: 50:8020i,8021a-d
TITLE: Histochemistry of enzymes in carcinoma of the mammary gland, uterus and prostate
AUTHOR(S): Hayashi, Masando; Shimoda, Kenji; Ogata, Kazuhiro; Takamori, Torao; Shiraogawa, Takuro; Kuroki, Seiichi; Uchida, Morio; Kawase, Osamu
CORPORATE SOURCE: Kumamoto Univ.
SOURCE: Kumamoto Medical Journal (1955), 8, 114-24
CODEN: KUMJAX; ISSN: 0023-5326
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB The original methods, except for the following modifications, were employed. In the demonstration of β-glucuronidase activities, fixation in 10% formol for 3 h at 4° followed by incubation for 3 h at 37° was used to avoid false reactions. Esterase activities were demonstrated in formol-fixed frozen sections instead of acetone-fixed paraffin sections. High activities of β-glucuronidase were observed in carcinomas of the mammary gland and low in those of the uterine cervix. Sulfatase usually showed moderate activities in both cases. β-Glucuronidase activity of innocent stratified squamous epithelium at portio vaginalis was very low, while it was moderate in the glandular epithelium of the mammary duct. Carcinoma simplex of the uterine cervix had certain histochem. resemblance to squamous cell carcinoma at that site, though seasoned with irregularities, and it was quite different from that of the mammary gland. High stromal reaction of β-glucuronidase in malignant tissue might be correlated with the increase of interfibrous substance of hyaluronic acid nature. The reaction of β-glucuronidase in the target organs showed considerably regular and characteristic ways of change as compared with other enzymes, suggesting its significance in the metabolism of hormones and in the cancerous transformation of the target organs. But sulfatase activities in tumors of these organs were not so high. In contrast to the results of Cohen et al., the nonspecific esterase activities of tumors of these organs often exhibited high levels when formol-fixed frozen section were used, but considerable fluctuations of activities were observed Cancer cells of the mammary gland, uterus and

prostate possessed high levels of phosphamidase. Fluctuations of the enzymic activities were considerable in phosphatase as well as in esterase in contrast to the other enzymes studied, and it was difficult to correlate the activities of both phosphatase and esterase with the degree of differentiation of tumors.

L14 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1953:32405 CAPLUS
DOCUMENT NUMBER: 47:32405
ORIGINAL REFERENCE NO.: 47:5515a-e
TITLE: Chemistry of connective tissue, polysaccharides
AUTHOR(S): Meyer, Karl
CORPORATE SOURCE: Columbia Univ.
SOURCE: Conf. on Connective Tissues, Trans. (1951), Volume Date 1950, 1, 88-100
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Connective tissue contains 5 different mucopolysaccharides: hyaluronic acid (I), chondroitin sulfate A (II) of hyaline cartilage, chondroitin sulfate B (III) of skin, chondroitin sulfate C (IV), and the sulfate ester (V) of corneal substantia propria. I is a polymer of a disaccharide composed of equimol. amts. of N-acetylglucosamine (VI) and gluconic acid with the reducing group on the VI moiety; it is found in vitreous humor, umbilical cord, synovial fluid, cock's comb, and some mesodermal tumors of the skin. Digestion of I by testicular hyaluronidase (VII) gives up to 70% yield of the basic oligosaccharide of I, and upon further attack by bacterial enzyme yields an increased amount of an unknown reducing disaccharide. There is evidence that the end product of I and VII may be of a higher order than a disaccharide. Natural I is of very high mol. weight and occurs as a polydisperse easily dissociated salt not bound to protein. The decrease of viscosity during isolation is due to the cleavage of anhydride bonds. II can be extracted from cartilage powder by concentrated $CaCl_2$ solution It has a mol. weight between 2 + 105 and 3 + 105 and consists of glucuronic acid, and N-acetylgalactosamine with a 6-SO_4 group. III and IV both contain equimol. amts. of N-acetylgalactosamine, glucuronic acid, and sulfate. III of $[\alpha]_D$ -50° is precipitated by 20% alc. and resists VII. IV of $[\alpha]_D$ -20° is precipitated by 50% alc. and is hydrolyzed by VII. III and IV are bound to protein (a mucoid of 35-40% carbohydrate content) which has an electrophoretic mobility of 8.1 + 10-5 at pH 8.5. The protein contains tyrosine and tryptophan in contrast to collagen. Umbilical cord contains no III but does yield large amts. of I and IV.

L14 ANSWER 14 OF 18 MEDLINE on STN
ACCESSION NUMBER: 2006255644 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16678050
TITLE: HYTAD1-p20: a new paclitaxel-hyaluronic acid hydrosoluble bioconjugate for treatment of superficial bladder cancer.
AUTHOR: Rosato Antonio; Banzato Alessandra; De Luca Gilda; Renier Davide; Bettella Fabio; Pagano Claudio; Esposito Giovanni; Zanovello Paola; Bassi PierFrancesco
CORPORATE SOURCE: Department of Oncology and Surgical Sciences, Oncology Section, University of Padua, Padua, Italy.. antonio.rosato@unipd.it
SOURCE: Urologic oncology, (2006 May-Jun) Vol. 24, No. 3, pp. 207-15.
Journal code: 9805460. ISSN: 1078-1439.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 200610
ENTRY DATE: Entered STN: 9 May 2006
Last Updated on STN: 20 Oct 2006
Entered Medline: 19 Oct 2006

AB OBJECTIVE: To report the development of a new water-soluble paclitaxel-hyaluronic acid bioconjugate, HYTAD1-p20, for intravesical treatment of superficial bladder cancer. MATERIALS AND METHODS: HYTAD1-p20 was synthesized by carboxyl esterification of hyaluronic acid with paclitaxel, and its physicochemical and biologic properties were characterized. RESULTS: Paclitaxel loading was optimized at 20% w/w; this procedure increased by 500-fold the paclitaxel concentration in the resulting water-soluble biomaterial. In vitro, HYTAD1-p20 exerted a much higher dose-dependent inhibitory effect against RT-4 and RT-112/84 bladder carcinoma cell growth than that of free drug, and directly interacted with CD44 expressed by bladder tumor cells. In vivo, results of pharmacokinetic studies performed in mice after bladder catheterization and intravesical instillation of HYTAD1-p20 disclosed that drug leakage was negligible during a 2-hour analysis. Histologic examination of drug-instilled bladders revealed that HYTAD1-p20 was extremely well tolerated, while paclitaxel alone produced mucosal disruption and submucosal infiltration of inflammatory cells. Treatment of severe combined immunodeficient mice bearing subcutaneous RT-112/84 tumors with maximum tolerated doses of bioconjugate or paclitaxel showed that HYTAD1-p20 exerted a therapeutic activity comparable to that of free drug. CONCLUSIONS: These data suggest that HYTAD1-p20 significantly improved results obtained with conventional paclitaxel in terms of hydrosolubility, in vitro activity against human bladder cancer cells, and in vivo biocompatibility. This bioconjugate is a potentially useful treatment for superficial urothelial malignancy.

L14 ANSWER 15 OF 18 MEDLINE on STN
ACCESSION NUMBER: 1999224662 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10209956
TITLE: Hyaluronic acid as drug delivery for sodium butyrate: improvement of the anti-proliferative activity on a breast-cancer cell line.
AUTHOR: Coradini D; Pellizzaro C; Miglierini G; Daidone M G; Perbellini A
CORPORATE SOURCE: Oncologia Sperimentale C, Istituto Nazionale per lo Studio e la Cura dei Tumori, Milan, Italy. coradini@istitutotumori.mi.it
SOURCE: International journal of cancer. Journal international du cancer, (1999 May 5) Vol. 81, No. 3, pp. 411-6.
Journal code: 0042124. ISSN: 0020-7136.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 11 May 1999
Last Updated on STN: 11 May 1999
Entered Medline: 29 Apr 1999

AB The potential clinical utility of sodium butyrate, a natural compound known to inhibit tumor-cell growth, is hampered by the difficulty of achieving effective in-vivo concentrations. The short half-life (about 5 minutes) of sodium butyrate results in rapid metabolism and excretion. To increase the availability of sodium butyrate over a longer period of time, we co-valently linked it to hyaluronic acid (a component of the extracellular matrix). Its major advantages as a drug carrier consist in its high biocompatibility and its ability to bind CD44, a specific membrane receptor frequently over-expressed on the tumor-cell surface. The degree of

substitution of hyaluronic acid with butyrate residues ranged from d.s.=0.10 to d.s.=2.24 (1.8-28.4% w/w). The biological activity of hyaluronic-acid-butyric-ester derivatives was evaluated in terms of the inhibition of the growth of the MCF7 cell line and compared with that of sodium butyrate. After 6 days of treatment, we observed a progressive improvement of the anti-proliferative activity up to d.s.=0.20; thereafter, the anti-proliferative effect of the ester derivatives decreased. Fluorescence microscopy showed that after 2 hr of treatment fluorescein-labelled compounds appeared to be almost completely internalized into MCF7 cells, expressing CD44 standard and variant isoforms. These findings indicate that hyaluronic acid could offer an important advantage in drug delivery, in addition to its biocompatibility: the ability to bind to CD44, which are known to be frequently over-expressed on the tumor-cell surface.

L14 ANSWER 16 OF 18 MEDLINE on STN
ACCESSION NUMBER: 97266064 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9111868
TITLE: CD44: structure, function, and association with the malignant process.
AUTHOR: Naor D; Sionov R V; Ish-Shalom D
CORPORATE SOURCE: Lautenberg Center for General and Tumor Immunology, Hebrew University-Hadassah Medical School, Jerusalem, Israel.
SOURCE: Advances in cancer research, (1997) Vol. 71, pp. 241-319. Ref: 489
Journal code: 0370416. ISSN: 0065-230X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199706
ENTRY DATE: Entered STN: 9 Jul 1997
Last Updated on STN: 29 Jan 1999
Entered Medline: 20 Jun 1997

AB CD44 is a ubiquitous multistructural and multifunctional cells surface adhesion molecule involved in cell-cell and cell-matrix interactions. Twenty exons are involved in the genomic organization of this molecule. The first five and the last 5 exons are constant, whereas the 10 exons located between these regions are subjected to alternative splicing, resulting in the generation of a variable region. Differential utilization of the 10 variable region exons, as well as variations in N-glycosylation, O-glycosylation, and glycosaminoglycanation (by heparan sulfate or chondroitin sulfate), generate multiple isoforms (at least 20 are known) of different molecular sizes (85-230 kDa). The smallest CD44 molecule (85-95 kDa), which lacks the entire variable region, is standard CD44 (CD44s). As it is expressed mainly on cells of lymphohematopoietic origin, CD44s is also known as hematopoietic CD44 (CD44H). CD44s is a single-chain molecule composed of a distal extracellular domain (containing, the ligand-binding sites), a membrane-proximal region, a transmembrane-spanning domain, and a cytoplasmic tail. The molecular sequence (with the exception of the membrane-proximal region) displays high interspecies homology. After immunological activation, T lymphocytes and other leukocytes transiently upregulate CD44 isoforms expressing variant exons (designated CD44v). A CD44 isform containing the last 3 exon products of the variable region (CD44V8-10, also known as epithelial CD44 or CD44E), is preferentially expressed on epithelial cells. The longest CD44 isoform expressing in tandem eight exons of the variable region (CD44V3-10) was detected in keratinocytes. Hyaluronic acid (HA), an important component of the extracellular matrix (ECM), is the principal, but by no means the only, ligand of CD44. Other CD44 ligands include the ECM components collagen, fibronectin, laminin, and chondroitin sulfate. Mucosal addressin, serglycin, osteopontin, and

the class II invariant chain (Ii) are additional, ECM-unrelated, ligands of the molecule. In many, but not in all cases, CD44 does not bind HA unless it is stimulated by phorbol esters, activated by agonistic anti-CD44 antibody, or deglycosylated (e.g., by tunicamycin). CD44 is a multifunctional receptor involved in cell-cell and cell-ECM interactions, cell traffic, lymph node homing, presentation of chemokines and growth factors to traveling cells, and transmission of growth signals. CD44 also participates in the uptake and intracellular degradation of HA, as well as in transmission of signals mediating hematopoiesis and apoptosis. Many cancer cell types as well as their metastases express high levels of CD44. Whereas some tumors, such as gliomas, exclusively express standard CD44, other neoplasms, including gastrointestinal cancer, bladder cancer, uterine cervical cancer, breast cancer and non-Hodgkin's lymphomas, also express CD44 variants. Hence CD44, particularly its variants, may be used as diagnostic or prognostic markers of at least some human malignant diseases. Furthermore, it has been shown in animal models that injection of reagents interfering with CD44-ligand interaction (e.g., CD44s- or CD44v-specific antibodies) inhibit local tumor growth and metastatic spread. These findings suggest that CD44 may confer a growth advantage on some neoplastic cells and, therefore, could be used as a target for cancer therapy. It is hoped that identification of CD44 variants expressed on cancer but not on normal cells will lead to the development of anti-CD44 reagents restricted to the neoplastic growth.

L14 ANSWER 17 OF 18 MEDLINE on STN
ACCESSION NUMBER: 93203668 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8095961
TITLE: CD44 antibody stimulates adhesion of peripheral blood T cells to keratinocytes through the leukocyte function-associated antigen-1/intercellular adhesion molecule-1 pathway.
AUTHOR: Bruynzeel I; Koopman G; van der Raaij L M; Pals S T; Willemze R
CORPORATE SOURCE: Department of Dermatology, Free University Hospital, Amsterdam, The Netherlands.
SOURCE: The Journal of investigative dermatology, (1993 Apr) Vol. 100, No. 4, pp. 424-8.
Journal code: 0426720. ISSN: 0022-202X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199304
ENTRY DATE: Entered STN: 7 May 1993
Last Updated on STN: 3 Feb 1997
Entered Medline: 22 Apr 1993

AB Close contact between T lymphocytes and keratinocytes is an important feature of many inflammatory skin diseases. In vitro studies showed that stimulation of keratinocytes with interferon-gamma or tumor necrosis factor-alpha and of T cells with phorbol esters results in a leukocyte function-associated antigen (LFA)-1/intercellular adhesion molecule (ICAM)-1-mediated adhesion. The present study was performed to investigate the role of the CD44 molecule in keratinocyte/T-cell binding. The CD44 class of lymphocyte adhesion receptors is involved in lymphocyte binding to high endothelial venules and to extracellular matrix compounds and is therefore important in lymphocyte recirculation and homing. Moreover, CD44 can act as a co-stimulating signal in T-cell activation and promotes homotypic adhesion of in vitro cultured CD3-stimulated T cells. Using a cell adhesion assay a sixfold increase in T-cell/keratinocyte adhesion was found after pre-incubating the T cells with anti-CD44. This increased adhesion was found to require an intact cytoskeleton, to be energy and magnesium dependent, and could be completely inhibited by anti-LFA-1 and anti-ICAM-1. Pretreatment of T cells with

hyaluronic acid, a ligand for CD44 and an extracellular matrix compound in the dermis and epidermis, did not affect T-cell/keratinocyte adhesion.

L14 ANSWER 18 OF 18 MEDLINE on STN
ACCESSION NUMBER: 77199465 MEDLINE
DOCUMENT NUMBER: PubMed ID: 141214
TITLE: Histochemical and ultrastructural studies in fibrodysplasia ossificans progressiva (myositis ossificans progressiva).
AUTHOR: Maxwell W A; Spicer S S; Miller R L; Halushka P V; Westphal M C; Setser M E
SOURCE: The American journal of pathology, (1977 Jun) Vol. 87, No. 3, pp. 483-98.
Journal code: 0370502. ISSN: 0002-9440.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 197707
ENTRY DATE: Entered STN: 14 Mar 1990
Last Updated on STN: 14 Mar 1990
Entered Medline: 18 Jul 1977

AB By light microscopy the subdermal nodule of a patient with fibrodysplasia ossificans progressiva (FOP) had a fibromatoid histologic appearance. The cytoplasm of the cells stained strongly for mannose-rich glycoprotein with the concanavalin A-horseradish peroxidase (con A-HRP) method. The tumors also exhibited abundant hyaluronidase-digestible mucopolysaccharide in the interstitium with various basic staining reagents. This material appeared to consist principally of hyaluronic acid or chondroitin sulfate with few or mainly masked sulfate esters. At the ultrastructural level, cells interpreted as the tumor cells in the subdermal nodule from the patient displayed extremely hyperplastic granular reticulum and well-developed Golgi elements and appeared very active in synthesis and secretion of protein. The material in the dilated cisternae of the granular reticulum stained for glycoprotein with the con-A-HRP method. Macrophages which comprised the other main cell type in the nodules commonly contacted the tumor cells and occasionally evidenced engulfment of these cells. The intercellular matrix of the nonossified subdermal nodule exhibited greatly increased mucosubstance and, by electron microscopy, showed an unusual network of dialyzed iron-reactive acid muco-substance in the interstitium.

L14 ANSWER 1 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:405314 CAPLUS
DOCUMENT NUMBER: 146:12762
TITLE: HYTAD1-p20: a new paclitaxel-hyaluronic acid hydrosoluble bioconjugate for treatment of superficial bladder cancer
AUTHOR(S): Rosato, Antonio; Banzato, Alessandra; De Luca, Gilda; Renier, Davide; Bettella, Fabio; Pagano, Claudio; Esposito, Giovanni; Zanovello, Paola; Bassi, PierFrancesco
CORPORATE SOURCE: Department of Oncology and Surgical Sciences, Oncology Section, University of Padova, Padua, Italy
SOURCE: Urologic Oncology: Seminars and Original Investigations (2006), 24(3), 207-215
CODEN: UOSOAA
PUBLISHER: Elsevier Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This paper reports the development of a new water-soluble paclitaxel-hyaluronic acid bioconjugate, HYTAD1-p20, for intravesical treatment of superficial bladder cancer. HYTAD1-p20 was synthesized by carboxyl esterification of hyaluronic acid with paclitaxel, and its physicochem. and biol. properties were characterized. Paclitaxel loading was optimized at 20% weight/weight; this procedure increased by 500-fold the paclitaxel concentration in the resulting water-soluble biomaterial. In vitro, HYTAD1-p20 exerted a much higher dose-dependent inhibitory effect against RT-4 and RT-112/84 bladder carcinoma cell growth than that of free drug, and directly interacted with CD44 expressed by bladder tumor cells. In vivo, results of pharmacokinetic studies performed in mice after bladder catheterization and intravesical instillation of HYTAD1-p20 disclosed that drug leakage was negligible during a 2-h anal. Histol. examination of drug-instilled bladders revealed that HYTAD1-p20 was extremely well tolerated, while paclitaxel alone produced mucosal disruption and submucosal infiltration of inflammatory cells. Treatment of severe combined immunodeficient mice bearing s.c. RT-112/84 tumors with maximum tolerated doses of bioconjugate or paclitaxel showed that HYTAD1-p20 exerted a therapeutic activity comparable to that of free drug. These data suggest that HYTAD1-p20 significantly improved results obtained with conventional paclitaxel in terms of hydrosoly., in vitro activity against human bladder cancer cells, and in vivo biocompatibility. This bioconjugate is a potentially useful treatment for superficial urothelial malignancy.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:591962 CAPLUS
DOCUMENT NUMBER: 143:91004
TITLE: Use of PSP64 and subfragments to suppress cell adhesion and migration, inhibit matrix metalloproteinase secretion, and treat cancer and other diseases
INVENTOR(S): Panchal, Chandra J.; Wu, Jinzi Jason; Beliveau, Richard; Ruiz, Marcia; Garde, Seema; Annabi, Borhane; Lamy, Sylvie; Bouzeghrane, Mounia; Daigneault, Luc; Hawkins, Robert
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 59 pp., Cont.-in-part of U.S. Ser. No. 948,229.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005147601	A1	20050707	US 2004-4270	20041202
CA 2441695	A1	20050326	CA 2003-2441695	20030926
US 2005096273	A1	20050505	US 2004-948229	20040924
AU 2005250059	A1	20051215	AU 2005-250059	20050321
CA 2567901	A1	20051215	CA 2005-2567901	20050321
WO 2005118623	A1	20051215	WO 2005-CA430	20050321
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1765852	A1	20070328	EP 2005-714663	20050321
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU				

PRIORITY APPLN. INFO.:		
CA 2003-2441695	A	20030926
US 2004-948229	A2	20040924
US 2004-857358	A	20040601
US 2004-4270	A	20041202
US 2004-4273	A	20041202
WO 2005-CA430	W	20050321

AB Matrix metalloproteinases (MMPs) play an important role in morphogenesis, angiogenesis, wound healing, and in certain disorders such as rheumatoid arthritis, tumor invasion and metastasis. MMPs are thought to be regulated by a variety of cytokines, growth factors, hormones and phorbol esters. This regulation occurs on three levels; alteration of gene expression, activation of the latent zymogen and inhibition by the tissue inhibitors of metalloproteinases (TIMP). We report here a new agent that regulates the level of MMPs, i.e., prostate secretory protein PSP94. Thus, PCK3145, a pentadecapeptide derived from PSP94, significantly decreased levels of MMP-9 in the blood of patients with metastatic adenocarcinoma of the prostate. A derivative of PCK3145 in which the 3 cysteine SH groups were acetaminomethylated, suppressed secretion of MMP from Mat-LyLu cells. This derivs. also decreased U-87 cell adhesion to hyaluronic acid as well as U-87 cell migration. Further effects of the PSP94 peptide derivative were increased CD44 cell surface shedding and induction of RhoA protein expression.

L14 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:583316 CAPLUS
DOCUMENT NUMBER: 142:147954
TITLE: Inhibition of hepatocellular carcinomas in vitro and hepatic metastases in vivo in mice by the histone deacetylase inhibitor HA-But
AUTHOR(S): Coradini, Danila; Zorzet, Sonia; Rossin, Raffaella; Scarlata, Ignazio; Pellizzaro, Cinzia; Turrin, Claudia; Bello, Michele; Cantoni, Silvia; Speranza, Annalisa; Sava, Gianni; Mazzi, Ulderico; Perbellini, Alberto
CORPORATE SOURCE: Unit of Biomolecular Determinants in Prognosis and Therapy, Experimental Department, Istituto Nazionale per lo Studio e la Cura dei Tumori, Milan, Italy
SOURCE: Clinical Cancer Research (2004), 10(14), 4822-4830

CODEN: CCREF4; ISSN: 1078-0432
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The purpose is to evaluate the CD44-mediated cellular targeting of HA-But, a hyaluronic acid esterified with butyric acid (But) residues, to hepatocellular carcinoma cell lines in vitro and to hepatic tumor metastases in vivo. In vitro, the CD44-dependent cytotoxicity in two human hepatocellular carcinoma cell lines (HepB3 and HepG2) with high and low CD44 expression was investigated; in vivo, the effect on liver metastases originating from intrasplenic implants of Lewis lung carcinoma (LL3) or B16-F10 melanoma in mice was compared with the pharmacokinetics of organ and tissue distribution using different routes of administration. HepB3 and HepG2 cell lines showed different expression of CD44 (78 and 18%, resp.), which resulted in a CD44-dependent HA-But inhibitory effect as demonstrated also by the uptake anal. performed using radiolabeled HA-But (99mTc-HA-But). Pharmacokinetic studies showed different rates of 99mTc-HA-But distribution according to the route of administration (i.v., i.p., or s.c.): very fast (a few minutes) after i.v. treatment, with substantial accumulation in the liver and spleen; relatively slow after i.p. or s.c. treatment, with marked persistence of the drug at the site of injection. The effect of s.c. and i.p. treatment with HA-But on liver metastases originating from intrasplenic implants of LL3 carcinoma or B16-F10 melanoma (both CD44-pos.: 68 and 87%, resp.), resulted in 87 and 100% metastases-free animals, resp. (regardless of the route of administration), and a significant prolongation of the life expectancy compared with control groups. HA-But tends to concentrate in the liver and spleen and appears to be a promising new drug for the treatment of intrahepatic tumor lesions.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:546533 CAPLUS
DOCUMENT NUMBER: 141:111540
TITLE: Mixed esters of hyaluronic acid with retinoic and butyric acids
INVENTOR(S): Perbellini, Alberto; Coradini, Danila
PATENT ASSIGNEE(S): Sintofarm S.P.A., Italy
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004056877	A1	20040708	WO 2003-EP14732	20031222
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2529816	A1	20040708	CA 2003-2529816	20031222
AU 2003294936	A1	20040714	AU 2003-294936	20031222
EP 1578803	A1	20050928	EP 2003-785916	20031222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

US 2006074048 A1 20060406 US 2005-540939 20050623

PRIORITY APPLN. INFO.: IT 2002-MI2745 A 20021223

WO 2003-EP14732 W 20031222

AB The present invention relates to mixed esters of hyaluronic acid, wherein the hydroxyl groups are partially esterified with retinoic and butyric acids. These mixed esters are characterized by specific degrees of esterification and by a high ratio between the degree of substitution with butyric acid and retinoic acid. They exhibit a high anti-proliferative activity associated with activation of cell differentiation, with consequent clin. relevance in the treatment of hyper-proliferative pathologies and in particular of solid and systemic tumors.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1999:246222 CAPLUS

DOCUMENT NUMBER: 131:110966

TITLE: Hyaluronic acid as drug delivery for sodium butyrate: improvement of the anti-proliferative activity on a breast-cancer cell line

AUTHOR(S): Coradini, Danila; Pellizzaro, Cinzia; Miglierini, Giuliana; Daidone, Maria Grazia; Perbellini, Alberto

CORPORATE SOURCE: Oncologia Sperimentale C, Istituto Nazionale per lo Studio e la Cura dei Tumori, Milan, 20133, Italy

SOURCE: International Journal of Cancer (1999), 81(3), 411-416
CODEN: IJCNAW; ISSN: 0020-7136

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The potential clin. utility of sodium butyrate, a natural compound known to inhibit tumor-cell growth, is hampered by the difficulty of achieving effective in-vivo concns. The short half-life (about 5 min) of sodium butyrate results in rapid metabolism and excretion. To increase the availability of sodium butyrate over a longer period of time, we co-valently linked it to hyaluronic acid (a component of the extracellular matrix). Its major advantages as a drug carrier consist in its high biocompatibility and its ability to bind CD44, a specific membrane receptor frequently over-expressed on the tumor -cell surface. The degree of substitution of hyaluronic acid with butyrate residues ranged from d.s. = 0.10 to d.s. = 2.24 (1.8-28.4% weight/weight). The biol. activity of hyaluronic-acid-butyric-ester derivs. was evaluated in terms of the inhibition of the growth of the MCF7 cell line and compared with that of sodium butyrate. After 6 days of treatment, we observed a progressive improvement of the anti-proliferative activity up to d.s. = 0.20; thereafter, the anti-proliferative effect of the ester derivs. decreased. Fluorescence microscopy showed that after 2 h of treatment fluorescein-labeled compds. appeared to be almost completely internalized into MCF7 cells, expressing CD44 standard and variant isoforms. These findings indicate that hyaluronic acid could offer an important advantage in drug delivery, in addition to its biocompatibility: the ability to bind to CD44, which are known to be frequently over-expressed on the tumor-cell surface.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1997:387785 CAPLUS

DOCUMENT NUMBER: 127:63472

TITLE: CD44: structure, function, and association with the malignant process

AUTHOR(S): Naor, David; Sionov, Ronit Vogt; Ish-Shalom, Dvorah
CORPORATE SOURCE: The Lautenberg Center for General and Tumor Immunology, The Hebrew University-Hadassah Medical School, Jerusalem, 91120, Israel
SOURCE: Advances in Cancer Research (1997), 71, 241-319
CODEN: ACRSAJ; ISSN: 0065-230X
PUBLISHER: Academic
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 388 refs. CD44 is a ubiquitous multi-structural and multifunctional cell surface adhesion mol. involved in cell-cell and cell-matrix interactions. Twenty exons are involved in the genomic organization of this mol. The first five and the last 5 exons are constant, whereas the 10 exons located between these regions are subjected to alternative splicing, resulting in the generation of a variable region. Differential utilization of the 10 variable region exons, as well as variations in N-glycosylation, O-glycosylation, and glycosaminoglycanation (by heparan sulfate or chondroitin sulfate), generate multiple isoforms (at least 20 are known) of different mol. sizes (85-230 kDa). The smallest CD44 mol. (85-95 kDa), which lacks the entire variable region, is standard CD44 (CD44s). As it is expressed mainly on cells of lymphohematopoietic origin, CD44s is also known as hematopoietic CD44 (CD44H). CD44s is a single-chain mol. composed of a distal extracellular domain (containing the ligand-binding sites), a membrane-proximal region, a transmembrane-spanning domain, and a cytoplasmic tail. The mol. sequence (with the exception of the membrane-proximal region) displays high interspecies homol. After immunol. activation, T lymphocytes and other leukocytes transiently upregulate CD44 isoforms expressing variant exons (designated CD44v). A CD44 isoform containing the last 3 exon products of the variable region (CD44V8-10, also known as epithelial CD44 or CD44E), is preferentially expressed on epithelial cells. The longest CD44 isoform expressing in tandem eight exons of the variable region (CD44V3-10) was detected in keratinocytes. Hyaluronic acid (HA), an important component of the extracellular matrix (ECM), is the principal, but by no means the only, ligand of CD44. Other CD44 ligands include the ECM components collagen, fibronectin, laminin, and chondroitin sulfate. Mucosal addressin, serglycin, osteopontin, and the class II invariant chain (Ii) are addnl., ECM-unrelated, ligands of the mol. In many, but not in all cases, CD44 does not bind HA unless it is stimulated by phorbol esters, activated by agonistic anti-CD44 antibody, or deglycosylated (e.g., by tunicamycin). CD44 is a multifunctional receptor involved in cell-cell and cell-ECM interactions, cell traffic, lymph node homing, presentation of chemokines and growth factors to traveling cells, and transmission of growth signals. CD44 also participates in the uptake and intracellular degradation of HA, as well as in transmission of signals mediating hematopoiesis and apoptosis. Many cancer cell types as well as their metastases express high levels of CD44. Where-as some tumors, such as gliomas, exclusively express standard CD44, other neoplasms, including gastrointestinal cancer, bladder cancer, uterine cervical cancer, breast cancer and non-Hodgkin's lymphomas, also express CD44 variants. Hence CD44, particularly its variants, may be used as diagnostic or prognostic markers of at least some human malignant diseases. Furthermore, it has been shown in animal models that injection of reagents interfering with CD44-ligand interaction (e.g., CD44s- or CD44v-specific antibodies) inhibit local tumor growth and metastatic spread. These findings suggest that CD44 may confer a growth advantage on some neoplastic cells and, therefore, could be used as a target for cancer therapy. It is hoped that identification of CD44 variants expressed on cancer but not on normal cells will lead to the development of anti-CD44 reagents restricted to the neoplastic growth.
REFERENCE COUNT: 382 THERE ARE 382 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:359752 CAPLUS
DOCUMENT NUMBER: 125:26304
TITLE: Hyaluronic acid and derivatives for modulation of cellular activity
INVENTOR(S): Asculai, Samuel Simon
PATENT ASSIGNEE(S): Hyal Pharmaceutical Corporation, Can.
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 24
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9606622	A1	19960307	WO 1995-CA477	19950811
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2131130	A1	19960301	CA 1994-2131130	19940830
CA 2145605	A1	19960928	CA 1995-2145605	19950327
IN 1995CA00916	A	20050304	IN 1995-CA916	19950807
AU 9531595	A	19960322	AU 1995-31595	19950811
EP 778776	A1	19970618	EP 1995-927605	19950811
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
HU 76846	A2	19971229	HU 1997-1507	19950811
JP 10504828	T	19980512	JP 1996-508371	19950811
ZA 9507223	A	19960401	ZA 1995-7223	19950829
CN 1130532	A	19960911	CN 1995-116995	19950829
CA 2268476	A1	19980430	CA 1996-2268476	19961018
AU 9672721	A	19980515	AU 1996-72721	19961018
AU 739701	B2	20011018		
EP 952855	A1	19991103	EP 1996-934250	19961018
EP 952855	B1	20050727		
R: DE, FR, GB, IT, SE				
NZ 335259	A	20001222	NZ 1996-335259	19961018
ZA 9608847	A	19970527	ZA 1996-8847	19961022
US 6475795	B1	20021105	US 1997-860696	19970616
US 2003036525	A1	20030220	US 2002-234355	20020904

PRIORITY APPLN. INFO.:

CA 1994-2131130	A	19940830
CA 1995-2145605	A	19950327
US 1995-468328	A2	19950606
WO 1995-CA477	W	19950811
WO 1996-CA700	A	19961018
US 1997-860696	A1	19970616

AB A method is provided for the modulation of cellular activity of tissue and cells expressing a high affinity cell-surface receptor for the hyaluronic acid, e.g. an adhesion mol. (e.g., ICAM-1, HARLEC, CD44) and a regulatory mol. (e.g., RHAMM) of a human. The method comprises the administration of a non-toxic effective amount of a form of hyaluronic acid [e.g., hyaluronic acid , a salt thereof, (e.g., sodium hyaluronate having a mol. weight of less than 750,000 daltons, (e.g., 225,000 daltons)), e.g. from Hyal Pharmaceutical Corp. within the range of 150,000-225,000 daltons and those disclosed in U. S. Patent Application 08/143,983, mol. weight fractions of a form of sodium hyaluronate (e.g., fractions disclosed in Canadian Letters Patent 1205031 (to Fidia)) such as those from 50,000-100,000 daltons, 250,000-350,000 daltons, and 500,000-730,000 daltons, or other fractions, homologues, analogs, derivs., complexes, esters, fragments,

and/or subunits of hyaluronic acid and/or combinations thereof] and/or hyaluronic acid-mimicking mols. to a human to modulate cellular activity of tissues and/or cells expressing a high affinity cell-surface receptor for hyaluronic acid , e.g., an adhesion mol. and a regulatory mol. in the human body, in a pharmaceutical excipient tolerable by the human (e.g., sterile water). Dosage amts. of pharmaceutical compns. are also disclosed. The methodol. of the invention is useful for the treatment of e.g. cold, stroke, inflammatory process, fibrosis, or cancer. Studies were performed to determine if accessible hyaluronic acid binding sites are present in tumor tissue in vivo, and the relation of these possible sites to previously described hyaluronic acid -binding proteins. Also, further evidence is presented that HARLEC/ICAM-1 is a receptor for hyaluronic acid, that hyaluronic acid also targets human tumors in nude rats, and that the targeting is mainly via binding to HARLEC/ICAM-1 on tumor endothelium.

L14 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1993:574227 CAPLUS
DOCUMENT NUMBER: 119:174227
TITLE: Hyaluronic acids for treatment of ischemia damage in tissues
INVENTOR(S): Falk, Rudolf E.; Asculai, Samuel S.; Klein, Ehud S.
PATENT ASSIGNEE(S): Norpharmco Inc., Can.
SOURCE: Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 24
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 557118	A1	19930825	EP 1993-301230	19930219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CA 2061567	A1	19930821	CA 1992-2061567	19920220
CA 2061567	C	19980203		
CA 2268476	A1	19980430	CA 1996-2268476	19961018
AU 9672721	A	19980515	AU 1996-72721	19961018
AU 739701	B2	20011018		
EP 952855	A1	19991103	EP 1996-934250	19961018
EP 952855	B1	20050727		
R: DE, FR, GB, IT, SE				
NZ 335259	A	20001222	NZ 1996-335259	19961018
ZA 9608847	A	19970527	ZA 1996-8847	19961022
US 6475795	B1	20021105	US 1997-860696	19970616
US 2003036525	A1	20030220	US 2002-234355	20020904

PRIORITY APPLN. INFO.:

CA 1992-2061567	A	19920220
WO 1996-CA700	A	19961018
US 1997-860696	A1	19970616

AB Hyaluronic acid (I), salts, homologs, analogs, derivs., complexes, esters, fragments, and units thereof are used for treatment of ischemia damage in tissues. Rats with liver-implanted mammary carcinoma were given i.v. injection of 3H 5-fluorouracil (II) and I. The uptake of II by tumor tissues was 40% more in I-treated animals than untreated ones.

L19 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1986:142259 CAPLUS
DOCUMENT NUMBER: 104:142259
TITLE: Mucopolysaccharides as neoplasm inhibitors
INVENTOR(S): Sakurai, Katsukiyo; Horie, Katsuyuki; Sakamoto, Takashi; Okuyama, Takashi
PATENT ASSIGNEE(S): Seikagaku Kogyo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 61000017	A	19860106	JP 1984-118283	19840611
JP 04056805	B	19920909		
PRIORITY APPLN. INFO.:			JP 1984-118283	19840611

AB Hyaluronic acid, crosslinked hyaluronic acid , and its salts are neoplasm inhibitors. Thus, hyaluronic acid (0.25 mg/mouse/day) in saline injected i.p. into mice bearing mammary gland tumor cells in blood prevented the metastasis of the tumor .

L22 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:34276 CAPLUS
DOCUMENT NUMBER: 146:128639
TITLE: Drug-containing photocrosslinked hyaluronic acid derivative gel
INVENTOR(S): Miyamoto, Kenji; Yasuda, Yousuke
PATENT ASSIGNEE(S): Seikagaku Corporation, Japan
SOURCE: PCT Int. Appl., 46pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007004675	A1	20070111	WO 2006-JP313412	20060705

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: JP 2005-198176 A 20050706

AB Disclosed is a drug-containing photocrosslinked hyaluronic acid derivative gel which is a photocrosslinked hyaluronic acid gel containing a drug introduced through covalent bonding and has such properties that the gel can be pressed out from an injecting device. The drug-containing photocrosslinked hyaluronic acid derivative gel can be pressed out, for example, through a 20-25 gauge injection needle at a pressure of 0.5-5 kg/cm2. For example, aminopropyl naproxen ester hydrochloride was prepared, and reacted with aminopropyl cinnamate-modified sodium hyaluronate to obtain a white solid naproxen-introduced photoreactive hyaluronic acid derivative The obtained compound was filled in a glass syringe with a phosphate buffer, and light irradiated to form a gel of the present invention.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1986:142259 CAPLUS
DOCUMENT NUMBER: 104:142259
TITLE: Mucopolysaccharides as neoplasm inhibitors
INVENTOR(S): Sakurai, Katsukiyo; Horie, Katsuyuki; Sakamoto, Takashi; Okuyama, Takashi
PATENT ASSIGNEE(S): Seikagaku Kogyo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 61000017	A	19860106	JP 1984-118283	19840611
JP 04056805	B	19920909		

PRIORITY APPLN. INFO.: JP 1984-118283 19840611

AB Hyaluronic acid, crosslinked hyaluronic acid , and its salts are neoplasm inhibitors. Thus, hyaluronic acid (0.25 mg/mouse/day) in saline injected i.p. into mice bearing mammary gland tumor cells in blood prevented the metastasis of the tumor .

L29 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:792089 CAPLUS
DOCUMENT NUMBER: 137:299928
TITLE: Pharmaceutical formulation for the treatment of gynecological diseases
INVENTOR(S): Yui, Nobuhiko; Murakami, Kouichi; Ooya, Tooru; Sato, Ikuo
PATENT ASSIGNEE(S): Chisso Corp., Japan
SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1249247	A2	20021016	EP 2002-7213	20020327
EP 1249247	A3	20030115		
EP 1249247	B1	20070228		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2002356447	A	20021213	JP 2002-80018	20020322
US 2002150605	A1	20021017	US 2002-108298	20020328
US 7041310	B2	20060509		

PRIORITY APPLN. INFO.: JP 2001-100426 A 20010330

AB This invention provides to a novel pharmaceutical formulation for the treatment of gynecol. diseases. The formulation comprises a drug for the intrauterine, intravaginal or intrapelvic administration, or for the administration into the ovarian endometrioma, and a biodegradable polymer comprising a chemical modified hyaluronic acid or a salt thereof prepared by O-acylating, alkoxylating or crosslinking a complex of hyaluronic acid or a salt thereof and a cationic compound in a nonaq. solvent. The preparation of the invention is preferably administered intrauterine, intravaginal, intrapelvic, and intratumor cavity. A suspension of distearyldimethylammonium chloride (DSC) in water was added to a solution of sodium hyaluronate (CHA) in water and the solution and the suspension were heated up to 45°. The resultant complex was recovered by centrifuging at 5000 rpm at room temperature and washed with warm water at 45°. After washing, the complex was lyophilized overnight and further vacuum-dried at 50° to give a CHA-DSC complex.

L29 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:477290 CAPLUS
DOCUMENT NUMBER: 131:256281
TITLE: Requirements for signal delivery through CD44: analysis using CD44-Fas chimeric proteins
AUTHOR(S): Ishiwatari-Hayasaka, Haruko; Fujimoto, Takashi; Osawa, Tomoko; Hirama, Toshiyasu; Toyama-Sorimachi, Noriko; Miyasaka, Masayuki
CORPORATE SOURCE: Department of Bioregulation, Biomedical Research Center, Osaka University Graduate School of Medicine, Suita, 565-0871, Japan
SOURCE: Journal of Immunology (1999), 163(3), 1258-1264
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English

AB CD44 is a transmembrane glycoprotein involved in various cell adhesion events, including lymphocyte migration, early hemopoiesis, and tumor metastasis. To examine the requirements of CD44 for signal

delivery through the extracellular domain, we constructed a chimeric CD44 protein fused to the intracellular domain of Fas on its C-terminus. In cells expressing the CD44-Fas fusion protein, apoptosis could be induced by treatment with certain anti-CD44 mAbs alone, especially those recognizing the epitope group d, which has been previously shown to play a role in ligand binding, indicating that ligation of a specific region of the CD44 extracellular domain results in signal delivery. Of note was that appropriate ligation of the epitope h also resulted in the generation of apoptotic signal, although this region was not thought to be involved in ligand binding. In contrast, the so-called blocking anti-CD44 mAbs (epitope group f) that can abrogate the binding of hyaluronate (HA) failed to induce apoptosis even after further crosslinking with the secondary Ab, indicating that a mere mAb-induced oligomerization of the chimeric proteins is insufficient for signal generation. However, these blocking mAbs were instead capable of inhibiting apoptosis induced by nonblocking mAb (epitope group h). Furthermore, a chimeric protein bearing a mutation in the HA binding domain and hence lacking the ability to recognize HA was incapable of mediating the mAb-induced apoptosis, suggesting that the functional integrity of the HA binding domain is crucial to the signal generation in CD44.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 1995:223909 CAPLUS

DOCUMENT NUMBER: 122:7432

TITLE: CD44 triggering enhances human NK cell cytotoxic functions

AUTHOR(S): Galandrini, Ricciarda; De Maria, Ruggero; Piccoli, Mario; Frati, Luigi; Santoni, Angela

CORPORATE SOURCE: Dep. Exptl. Med., Univ. Rome, Rome, Italy

SOURCE: Journal of Immunology (1994), 153(10), 4399-407
CODEN: JOIMA3; ISSN: 0022-1767

PUBLISHER: American Association of Immunologists

DOCUMENT TYPE: Journal

LANGUAGE: English

AB CD44, a major hyaluronate receptor, is involved in a variety of lymphocyte functions including lympho-hemopoiesis, adhesion to high endothelial venules or the extracellular matrix, and T cell activation. Here the authors investigated the ability of CD44 to affect the cytotoxic functions of human NK cells. Ligation of CD44 by selected mAb (J173 and F10442) resulted in a rapid, dose response-dependent enhancement of NK cytotoxic activity against a panel of tumor target cells that varied in their sensitivity to NK killing. Neither enhanced killing against NK-resistant target cells nor CD44 mAb-mediated redirected lysis was observed CD44 crosslinking also was found to up-regulate CD16-mediated lysis. To investigate the early biochem. events that occur after CD44 ligation, the authors found that optimal crosslinking conditions induce a rapid increase of intracellular free calcium levels, which is abrogated by extracellular Ca2+ chelation. Moreover, enhanced and more sustained Ca2+ rise resulted from CD16 and CD44 co-engagement. In contrast, no inositol 1,4,5-triphosphate generation was found after optimal CD44 crosslinking. Thus, although CD44 is not capable of delivering a lytic signal in human NK cells, it co-activates spontaneous or CD16-mediated NK cytotoxicity. The variation in intracellular free calcium may be one of the signals that account for the costimulation of the lytic activity.

L32 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:694981 CAPLUS
DOCUMENT NUMBER: 143:482971
TITLE: Implantation of preadipocyte-loaded hyaluronic acid-based scaffolds into nude mice to evaluate potential for soft tissue engineering
AUTHOR(S): Hemmrich, Karsten; von Heimburg, Dennis; Rendchen, Raoul; Di Bartolo, Chiara; Milella, Eva; Pallua, Norbert
CORPORATE SOURCE: Department of Plastic Surgery and Hand Surgery, University Hospital of the Aachen University of Technology, Aachen, D-52057, Germany
SOURCE: Biomaterials (2005), 26(34), 7025-7037
CODEN: BIMADU; ISSN: 0142-9612
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The reconstruction of soft tissue defects following extensive deep burns or tumor resections remains an unresolved problem in plastic and reconstructive surgery since adequate implant materials are still not available. Preadipocytes, immature precursor cells found between mature adipocytes in adipose tissue, are a potential material for soft tissue engineering since they can proliferate and differentiate into adipose tissue after transplantation. In previous studies, the authors identified hyaluronan benzyl ester (HYAFF-11) sponges to be promising carrier matrixes. This study now evaluates, in vitro and in vivo, a new sponge architecture with pores of 400 μm either made of plain HYAFF-11 or HYAFF-11 coated with the extracellular matrix glycosaminoglycan hyaluronic acid. Human preadipocytes were isolated, seeded onto carriers and implanted into nude athymic mice. Explants harvested after 3, 8, and 12 wk were examined for macroscopical appearance, thickness, weight, pore structure, histol., and immunohistochem. Compared to previous studies, the authors found better penetration of cells into both types of scaffolds, with more extensive formation of new vessels throughout the construct but with only minor adipose tissue. The authors' encouraging results contribute towards a better seeded and vascularized scaffold but also show that the enhancement of adipogenic conversion of preadipocytes remains a major task for further in vivo expts.
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L32 ANSWER 2 OF 2 MEDLINE on STN
ACCESSION NUMBER: 2005400405 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15964623
TITLE: Implantation of preadipocyte-loaded hyaluronic acid-based scaffolds into nude mice to evaluate potential for soft tissue engineering.
AUTHOR: Hemmrich Karsten; von Heimburg Dennis; Rendchen Raoul; Di Bartolo Chiara; Milella Eva; Pallua Norbert
CORPORATE SOURCE: Department of Plastic Surgery and Hand Surgery, Burn Centre, University Hospital of the Aachen University of Technology, Germany.
SOURCE: Biomaterials, (2005 Dec) Vol. 26, No. 34, pp. 7025-37.
Journal code: 8100316. ISSN: 0142-9612.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (EVALUATION STUDIES)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200512
ENTRY DATE: Entered STN: 3 Aug 2005

Last Updated on STN: 15 Dec 2005
Entered Medline: 7 Dec 2005

AB The reconstruction of soft tissue defects following extensive deep burns or tumor resections remains an unresolved problem in plastic and reconstructive surgery since adequate implant materials are still not available. Preadipocytes, immature precursor cells found between mature adipocytes in adipose tissue, are a potential material for soft tissue engineering since they can proliferate and differentiate into adipose tissue after transplantation. In previous studies, we identified hyaluronan benzyl ester (HYAFF 11) sponges to be promising carrier matrices. This study now evaluates, in vitro and in vivo, a new sponge architecture with pores of 400 microm either made of plain HYAFF 11 or HYAFF 11 coated with the extracellular matrix glycosaminoglycan hyaluronic acid. Human preadipocytes were isolated, seeded onto carriers and implanted into nude athymic mice. Explants harvested after 3, 8, and 12 weeks were examined for macroscopical appearance, thickness, weight, pore structure, histology, and immunohistochemistry. Compared to previous studies, we found better penetration of cells into both types of scaffolds, with more extensive formation of new vessels throughout the construct but with only minor adipose tissue. Our encouraging results contribute towards a better seeded and vascularised scaffold but also show that the enhancement of adipogenic conversion of preadipocytes remains a major task for further in vivo experiments.

L33 ANSWER 5 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1144397 CAPLUS
DOCUMENT NUMBER: 146:12983
TITLE: Antitumor sustained-release injection containing platinum compound and/or its synergistic agent
INVENTOR(S): Kong, Qinglun
PATENT ASSIGNEE(S): Jinan Shuaihua Pharmaceutical Science and Technology Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 29pp. CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1850043	A	20061025	CN 2006-10200142	20060220
PRIORITY APPLN. INFO.:			CN 2006-10200142	20060220

AB The sustained-release injection is comprised of (A) sustained-release microsphere comprising antitumor effective constituent 0.5-60, sustained-release adjuvant 41-99.9 and suspending agent 0.0-30%; and (B) solvent. The antitumor effective constituent is selected from platinum compound and/or its synergistic agent which is selected from phosphoinositide-3-kinase inhibitor, guanine analog, tetrazine compound and/or platinum compound Said platinum drug is selected from cisplatin, carboplatin, ormaplatin, dexormaplatin, hetaplatin, lobaplatin, nedaplatin or oxaliplatin. Said phosphoinositide-3-kinase inhibitor is selected from one of 7-hydroxyl-staurosporine, 7-oxy-alkyl-staurosporine, β-methoxyl staurosporine, etc., or the mixture thereof. Said guanine analog is selected from benzyl guanine, O6-benzyl guanine, O6-Bu guanine, O6-Me guanine, O6-alkyl guanine, etc. Said tetrazine compound is selected from imidazo tetrazine, imidazo pyrazine, 1-hydrogen-imidazo[b]pyrazine, imidazopyridine, 1-hydrogen-imidazo[1,2-a]pyridine, procarbazine, mitozolomide, dacarbazine, and temozolomide. The sustained-release adjuvant is selected from one of (a) polylactic acid; (b) Polyglycolic acid-hydroxy acetic acid copolymer; (c) polifeprosan; (d) ethene-vinyl acetate copolymer; (e) difatty acid-sebacic acid copolymer; (f) poly(erucic acid dimer-sebacic acid) copolymer; (g) poly(fumaric acid-sebacic acid) copolymer, xylitol, oligosaccharide, chondroitin, chitin, hyaluronic acid, collagens, etc.; or the mixture thereof. The suspending agent is one of (a) 0.5-3.0 % (sodium) CM-cellulose; (b) 5-15 % mannitol; (c) 5-15 % sorbitol; (d) 0.1-1.5 % surfactant; (e) 0.1-0.5 % tween 20; (f) (iodine) glycerin, dimethicone, propylene glycol, or carbomer; (g) 0.5-5 % sodium CM-cellulose + 0.1-0.5 % tween 80; (h) 5-20 % mannitol + 0.1-0.5 % tween 80; or (i) 0.5-5 % sodium CM-cellulose + 5-20 % sorbitol + 0.1-0.5 % tween 80, or the mixture thereof.

L33 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1144333 CAPLUS
DOCUMENT NUMBER: 146:12981
TITLE: Compound platinum antitumor sustained-release injection
INVENTOR(S): Kong, Qinglun
PATENT ASSIGNEE(S): Jinan Shuaihua Pharmaceutical Science and Technology Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 35pp. CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1850039	A	20061025	CN 2006-10200138	20060220

PRIORITY APPLN. INFO.: CN 2006-10200138 20060220

AB The sustained-release injection is comprised of (A) sustained-release microsphere comprising antitumor effective constituent 0.5-60, sustained-release adjuvant 40-99% and suspending agent 0.0-30%; and (B) solvent. The antitumor effective constituent is selected from platinum drug and/or its synergistic agent which is selected from phosphoinositide-3-kinase inhibitor, pyrimidine analog, and/or DNA repairase inhibitor. The platinum drug is selected from cisplatin, carboplatin, ormaplatin, dexormaplatin, hetaplatin, lobaplatin, nedaplatin or oxaliplatin. The phosphoinositide-3-kinase inhibitor is selected from one of 7-hydroxyl-staurosporine, 7-oxy-alkyl-staurosporine, β-methoxyl staurosporine, etc., or the mixture thereof. The pyrimidine analog is selected from one of 04-benzyl folic acid, 2,4,5-triamino-6-benzyloxy pyrimidine, 2,4-diamino-6-benzyloxy-5-nitrosopyrimidine, 2-amino-O-4-benzyl pteridine, etc., or the mixture thereof. The DNA repairase inhibitor is selected from one of (a) imidazo pyrazine, imidazopyridine, wortmannin, Benzochromanone, 2-(morpholine-4-yl)-benzo[h]chomen-4-one, etc.; (b) 3-aminobenzamide, benzamide, 3,4-dihydro-5-methoxyisoquinolin-1(2H)-benzamide, etc.; and (c) aminotriazole, DL-buthionine(S,R)-sulfoximine, calvatic acid, S-hexyl glutathione, etc. The sustained-release adjuvant is selected from one of (a) polylactic acid; (b) Polyglycolic acid-hydroxy acetic acid copolymer; (c) polifeprosan; (d) ethene-vinyl acetate copolymer; (e) difatty acid-sebacic acid copolymer; (f) poly(erucic acid dimer-sebacic acid) copolymer; (g) poly(fumaric acid-sebacic acid) copolymer; (h) sodium CM-cellulose, hydroxypropyl cellulose, xylitol, oligosaccharide, chondroitin, chitin, hyaluronic acid, collagens, etc.; or the mixture thereof. The suspending agent is one of (a) 0.5-3.0 % (sodium) CM-cellulose; (b) 5-15 % mannitol; (c) 5-15 % sorbitol; (d) 0.1-1.5 % surfactant; (e) 0.1-0.5 % tween 20; (f) (iodine) glycerin, dimethicone, propylene glycol, or carbomer; (g) 0.5-5 % sodium CM-cellulose + 0.1-0.5 % tween 80; (h) 5-20 % mannitol + 0.1-0.5 % tween 80; or (i) 0.5-5 % sodium CM-cellulose + 5-20 % sorbitol + 0.1-0.5 % tween 80, or the mixture thereof.

L33 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1112813 CAPLUS
DOCUMENT NUMBER: 145:495542
TITLE: Antitumor sustained-release injection containing taxane and its synergistic agent
INVENTOR(S): Liu, Yuyan
PATENT ASSIGNEE(S): Jinan Kangquan Pharmaceutical Science and Technology Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 35pp. CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1846687	A	20061018	CN 2006-10200112	20060210

PRIORITY APPLN. INFO.: CN 2006-10200112 20060210

AB The patent antitumor sustained-release injection is comprised of (A) sustained-release microsphere comprising antitumor effective constituent 0.5-60%, sustained-release adjuvant 40-99% and suspending agent 0.0-30.0%; and (B) solvent. The antitumor effective constituent is taxane and taxane synergistic agent which is selected from phosphoinositide-3-kinase inhibitor, pyrimidine analogs and/or DNA repair

enzyme inhibitor. Said taxane is selected from taxol, docetaxel, paclitaxel-2'-hydroxy, 10-deacetylbaccatin III, and 7-epi-taxol. Said phosphoinositide-3-kinase inhibitor is selected from one of 7-hydroxyl-staurosporine, 7-oxy-alkyl-staurosporine, β-methoxyl staurosporine, etc., or the mixture thereof. Said pyrimidine analog is selected from one of 04-benzyl folic acid, 2,4,5-triamino-6-benzyloxy pyrimidine, 2,4-diamino-6-benzyloxy -5-nitrosopyrimidine, 2-amino-O-4-benzyl pteridine, etc., or the mixture thereof. Said DNA repair enzyme inhibitor is selected from one of (a) imidazo pyrazine, imidazopyridine, Wortmannin, Benzochromenone, 2-(morpholine-4-yl)-benzo[h]chomen-4-one, etc.; (b) 3-aminobenzamide, benzamide, 3,4-dihydro-5-methoxyisoquinolin-1(2H)-benzamide, etc.; and (c) aminotriazole, DL-buthionine(S,R)-sulfoximine, Calvatic acid, S-hexyl glutathione, etc. The sustained-release adjuvant is selected from one of (a) polylactic acid; (b) Polyglycolic acid-hydroxy acetic acid copolymer; (c) polifeprosan; (d) ethene-vinyl acetate copolymer; (e) difatty acid-sebacic acid copolymer; (f) poly(erucic acid dimer-sebacic acid) copolymer; (g) poly(fumaric acid-sebacic acid) copolymer, xylitol, oligosaccharide, chondroitin, chitin, hyaluronic acid, collagens, gelatin, etc.; or the mixture thereof. The suspending agent is one of (a) 0.5-3.0 % (sodium) CM-cellulose; (b) 5-15 % mannitol; (c) 5-15 % sorbitol; (d) 0.1-1.5 % surfactant; (e) 0.1-0.5 % tween 20; (f) (iodine) glycerin, dimethicone, propylene glycol, or carbomer; (g) 0.5-5 % sodium CM-cellulose + 0.1-0.5 % tween 80; (h) 5-20 % mannitol + 0.1-0.5 % tween 80; or (i) 0.5-5 % sodium CM-cellulose + 5-20 % sorbitol + 0.1-0.5 % tween 80. Said sustained-release preparation can reduce toxic reaction, at the same time can increase selectively drug concentration, and enhance therapeutic effectiveness.

L33 ANSWER 8 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1112810 CAPLUS
DOCUMENT NUMBER: 145:495541
TITLE: Antitumor sustained-release injection containing taxane and its synergistic agent
INVENTOR(S): Liu, Yuyan
PATENT ASSIGNEE(S): Jinan Kangquan Pharmaceutical Science and Technology Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 34pp. CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1846686	A	20061018	CN 2006-10200110	20060210
PRIORITY APPLN. INFO.:			CN 2006-10200110	20060210

AB The patent antitumor sustained-release injection is comprised of (A) sustained-release microsphere comprising antitumor effective constituent 0.5-60%, sustained-release adjuvant 40-99% and suspending agent 0.0-30.0%; and (B) solvent. The antitumor effective constituent is taxane and taxane synergistic agent which is selected from topoisomerase inhibitors, guanine analogs, tetrazine compds., and platinum compds. Said topoisomerase inhibitor is selected from one of camptothecin, hydroxycamptothecine, lurtotecan, topotecan, irinotecan, etc., or the mixture thereof. Said guanine drug is selected from benzyl guanine, O6-benzyl guanine, O6-Bu guanine, O6-Me guanine, O6-alkyl guanine, etc. or the mixture thereof. Said platinum compound is selected from one of cisplatin, cycloplatin, sunplatinum, dacarbazine, nedaplatin, ormaplatin, zeniplatin, etc. Said tetrazine compound is selected from one of imidazotetrazine, imidazopyridine, 1-hydrogen-imidazo[b]pyrazine, imidazopyridine, 1-hydrogen-imidazo[1,2-a]pyridinium, procarbazine, mitozolomide, dacarbazine, temozolomide, or

the mixture thereof. Said platinum compound is selected from one of cisplatin, cycloplatin, sunplatinum, dacarbazine, nedaplatin, or ormaplatin. The sustained-release adjuvant is selected from one of (a) polylactic acid; (b) Polyglycolic acid-hydroxy acetic acid copolymer; (c) polifeprosan; (d) ethene-vinyl acetate copolymer; (e) difatty acid-sebacic acid copolymer; (f) poly(erucic acid dimer-sebacic acid) copolymer; (g) poly(fumaric acid-sebacic acid) copolymer, xylitol, oligosaccharide, chondroitin, chitin, hyaluronic acid, collagens, gelatin, etc.; or the mixture thereof. The suspending agent is one of (a) 0.5-3.0 % (sodium) CM-cellulose; (b) 5-15 % mannitol; (c) 5-15 % sorbitol; (d) 0.1-1.5 % surfactant; (e) 0.1-0.5 % tween 20; (f) (iodine) glycerin, dimethicone, propylene glycol, or carbomer; (g) 0.5-5 % sodium CM-cellulose + 0.1-0.5 % tween 80; (h) 5-20 % mannitol + 0.1-0.5 % tween 80; or (i) 0.5-5 % sodium CM-cellulose + 5-20 % sorbitol + 0.1-0.5 % tween 80. Said sustained-release preparation can reduce toxic reaction, at the same time can increase selectively drug concentration, and enhance therapeutic effectiveness.

L33 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1112807 CAPLUS
DOCUMENT NUMBER: 145:495540
TITLE: Antitumor sustained-release injection containing bendamustine and its synergistic agent
INVENTOR(S): Kong, Qingxia
PATENT ASSIGNEE(S): Jinan Shuaihua Pharmaceutical Science and Technology Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 28pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1846685	A	20061018	CN 2006-10200078	20060125

PRIORITY APPLN. INFO.: CN 2006-10200078 20060125

AB The title antitumor sustained-release injection is comprised of (A) sustained-release microsphere comprising antitumor effective constituent 0.5-60%, sustained-release adjuvant 40-99% and suspending agent 0.0-30.0%; and (B) solvent. The antitumor effective constituent is bendamustine or the combination of bendamustine and its synergistic agent which is selected from topoisomerase inhibitors, guanine analogs, tetrazine compds., and platinum compds. Said platinum compound is selected from one of cisplatin, cycloplatin, sunplatinum, dacarbazine, nedaplatin, ormaplatin, zeniplatin, etc. Said topoisomerase inhibitor is selected from one of camptothecin, hydroxycamptothecine, lurtotecan, topotecan, irinotecan, etc., or the mixture thereof. Said guanines drug is selected from benzyl guanine, O6-benzyl guanine, O6-Bu guanine, O6-Me guanine, O6-alkyl guanine, etc. or the mixture thereof. Said tetrazine compound is selected from one of imidazo tetrazine, imidazopyridine, 1-hydrogen-imidazo[b]pyrazine, imidazopyridine, 1-hydrogen-imidazo[1,2-a]pyridinium, procarbazine, mitozolomide, dacarbazine, temozolomide, or the mixture thereof. Said platinum compound is selected from one of cisplatin, cycloplatin, sunplatinum, dacarbazine, nedaplatin, or ormaplatin, etc. The sustained-release adjuvant is selected from one of (a) polylactic acid; (b) Polyglycolic acid-hydroxy acetic acid copolymer; (c) polifeprosan; (d) ethene-vinyl acetate copolymer; (e) difatty acid-sebacic acid copolymer; (f) poly(erucic acid dimer-sebacic acid) copolymer; (g) poly(fumaric acid-sebacic acid) copolymer, xylitol, oligosaccharide, chondroitin, chitin, hyaluronic acid, collagens, gelatin, etc.; or the mixture thereof. The suspending agent is one of (a) 0.5-3.0 % (sodium) CM-cellulose; (b) 5-15 % mannitol; (c) 5-15 % sorbitol; (d) 0.1-1.5 %

surfactant; (e) 0.1-0.5 % tween 20; (f) (iodine) glycerin, dimethicone, propylene glycol, or carbomer; (g) 0.5-5 % sodium CM-cellulose + 0.1-0.5 % tween 80; (h) 5-20 % mannitol + 0.1-0.5 % tween 80; or (i) 0.5-5 % sodium CM-cellulose + 5-20 % sorbitol + 0.1-0.5 % tween 80. Said sustained-release preparation can reduce toxic reaction, at the same time can increase selectively drug concentration, and enhance therapeutic effectiveness.

L33 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:220544 CAPLUS
DOCUMENT NUMBER: 144:338105
TITLE: Angiostatic and guanine analog composite antitumor implanting agent
INVENTOR(S): Kong, Qingzhong; Sun, Juan; Chen, Ying
PATENT ASSIGNEE(S): Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 20 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1733306	A	20060215	CN 2005-10044376	20050805
PRIORITY APPLN. INFO.:			CN 2005-10044376	20050805

AB The antitumor implanting agent is composed of angiostatic agent 5-30, antitumor agent 5-30, and medical adjuvant to 100%. The angiostatic agent is carboxyamidotriazole, thalidomide, linomide, angiostatin, endostatin, vascular endothelial growth factor receptor inhibitor, imatinib mesylate, semaxanib, gefitinib, erlotinib, etc. The antitumor agent is guanine, O6-benzylguanine, O6-butylguanine, O6-methylguanine, O6-alkylguanine, 2-amino-6-oxypurine, O6-benzyl-2'-deoxyguanosine, 8-amino-O6-benzylguanine, 8-hydroxy-O6-benzylguanine, 8-bromo-O6-benzylguanine, etc. The medical adjuvant is polylactic acid, ethylene-vinyl acetate copolymer, xylitol, oligosaccharide, chitin, hyaluronic acid, chondroitin sulfate, etc. The dosage form of the antitumor implanting agent is suspension, release sustaining agent, implant, and release sustaining implant. The systemic toxic reaction of the antitumor agent is decreased and the local concentration of the antitumor agent is increased by local administration, so the pharmacol. effect is increased.

L33 ANSWER 1 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1221768 CAPLUS
DOCUMENT NUMBER: 146:50226
TITLE: Sustained-release microsphere injection formulation of platinum combination with their synergistic agents from phosphoinositide-3-kinase inhibitor, pyrimidine analogs, and DNA repairase inhibitor
INVENTOR(S): Kong, Qingzhong; Zhang, Hongjun; Yu, Jianjiang
PATENT ASSIGNEE(S): Shandong Lan-Jin Bioengineering Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 33pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1861050	A	20061115	CN 2006-10200585	20060621

PRIORITY APPLN. INFO.: CN 2006-10200585 20060621

AB The invention provides a novel sustained-release microsphere injection formulation of platinum combination with their synergistic agents from phosphoinositide-3-kinase inhibitor, pyrimidine analogs, and DNA repairase inhibitor. The patent antitumor sustained-release injection is comprised of (A) sustained-release microsphere comprising antitumor effective constituent 0.5-60 wt%, and sustained-release adjuvant 40-99 wt%, and suspending agent 0.0-30 wt%; and (B) solvent. The antitumor effective constituent is platinum compds. and/or their synergistic agents from phosphoinositide-3-kinase inhibitor, pyrimidine analog, and/or DNA repairase inhibitor. The platinum compds. are selected from selected from sunpla, eptaplatin, bicycloplatin, citricplatin, and picoplatin. The phosphoinositide-3-kinase inhibitor is selected from one of 7-hydroxyl-staurosporine, 7-oxy-alkyl-staurosporine, β-methoxyl staurosporine, etc., or the mixture thereof. The pyrimidine analog is selected from one of 04-benzyl folic acid, 2,4,5-triamino-6-benzyloxy pyrimidine, 2,4-diamino-6-benzyloxy -5-nitrosopyrimidine, 2-amino-O-4-benzyl pteridine, etc., or the mixture thereof. The DNA repairase inhibitor is selected from one of (a) 2-(morphol-4-yl)-benzo[h]chromone-4-one, 2-(4-morpholinyl)-8-Ph chromone, etc.; (b) 3-aminobenzamide, benzamide, 3,4-dihydro methoxyisoquinolin-1(2H)-benzamide, etc.; and (c) aminotriazole, DL-buthionine(S,R)-sulfoximine, calvatic acid, S-hexyl glutathione, etc. The sustained-release adjuvant is selected from one of (a) polylactic acid; (b) Polyglycolic acid-hydroxy acetic acid copolymer; (c) polifeprosan; (d) ethene-vinyl acetate copolymer; (e) difatty acid-sebacic acid copolymer; (f) poly(erucic acid dimer-sebacic acid) copolymer; (g) poly(fumaric acid-sebacic acid) copolymer; (h) sodium CM-cellulose, hydroxypropyl cellulose, xylitol, oligosaccharide, chondroitin, chitin, hyaluronic acid, collagens, etc.; or (i) racemic polylactic acid, etc., or the mixture thereof. The suspending agent is one of (a) 0.5-3.0 % (sodium) CM-cellulose; (b) 5-15 % mannitol; (c) 5-15 % sorbitol; (d) 0.1-1.5 % surfactant; (e) 0.1-0.5 % tween 20; (f) (iodine) glycerin, dimethicone, propylene glycol, or carbomer; (g) 0.5-5 % sodium CM-cellulose + 0.1-0.5 % tween 80; (h) 5-20 % mannitol + 0.1-0.5 % tween 80; or (i) 0.5-5 % sodium CM-cellulose + 5-20 % sorbitol + 0.1-0.5 % tween 80. Said sustained-release preparation can reduce toxic reaction, at the same time can increase selectively drug concentration, and enhance therapeutic effectiveness.

L33 ANSWER 2 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1221763 CAPLUS
DOCUMENT NUMBER: 146:50225

TITLE: Sustained-release microsphere injection formulation of gemcitabine combination with phosphoinositide-3-kinase inhibitor, pyrimidine analog, and/or DNA repairase inhibitor
INVENTOR(S): Kong, Qingzhong; Sun, Juan; Liu, Yuyan; Song, Bangqiang
PATENT ASSIGNEE(S): Shandong Lan-Jin Bioengineering Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 34pp. CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1861049	A	20061115	CN 2006-10200256	20060317
PRIORITY APPLN. INFO.:			CN 2006-10200256	20060317

AB The patent antitumor sustained-release injection is comprised of (A) sustained-release microspheres comprising antitumor effective constituent 0.5-60 wt%, and sustained-release adjuvant 40-99 wt%, and suspending agent 0.0-30 wt%; and (B) solvent. The antitumor effective constituent is an antimetabolic drug and/or its synergistic agent from phosphoinositide-3-kinase inhibitor, pyrimidine analog, and/or DNA repairase inhibitor. The antimetabolic antitumor drug is selected from alimta, alimta disodium, carmofur, tegafur, zalcitabine, etc. The phosphoinositide-3-kinase inhibitor is selected from one of 7-hydroxyl-staurosporine, 7-oxy-alkyl-staurosporine, β-methoxyl staurosporine, etc., or the mixture thereof. The pyrimidine analog is selected from one of O-4-benzyl folic acid, 2,4,5-triamino-6-benzyloxy pyrimidine, 2,4-diamino-6-benzyloxy-5-nitrosopyrimidine, 2-amino-O-4-benzyl pteridine, etc., or the mixture thereof. The DNA repairase inhibitor is selected from one of (a) 2-(morphol-4-yl)-benzo[h]chromone-4-one, 2-(4-morpholinyl)-8-Ph chromone, etc.; (b) 3-aminobenzamide, benzamide, 3,4-dihydro methoxyisoquinolin-1(2H)-benzamide, etc.; and (c) aminotriazole, DL-buthionine(S,R)-sulfoximine, calvatic acid, S-hexyl glutathione, etc. The sustained-release adjuvant is selected from one of (a) polylactic acid; (b) Polyglycolic acid-hydroxy acetic acid copolymer; (c) polifeprosan; (d) ethene-vinyl acetate copolymer; (e) difatty acid-sebacic acid copolymer; (f) poly(erucic acid dimer-sebacic acid) copolymer; (g) poly(fumaric acid-sebacic acid) copolymer; (h) sodium CM-cellulose, hydroxypropyl cellulose, xylitol, oligosaccharide, chondroitin, chitin, hyaluronic acid, collagens, etc.; or (i) racemic polylactic acid, etc., or the mixture thereof. The suspending agent is one of (a) 0.5-3.0% (sodium) CM-cellulose; (b) 5-15% mannitol; (c) 5-15% sorbitol; (d) 0.1-1.5% surfactant; (e) 0.1-0.5% Tween 20; (f) (iodine) glycerin, dimethicone, propylene glycol, or carbomer; (g) 0.5-5% sodium CM-cellulose + 0.1-0.5% Tween 80; (h) 5-20% mannitol + 0.1-0.5% Tween 80; or (i) 0.5-5% sodium CM-cellulose + 5-20% sorbitol + 0.1-0.5% Tween 80. Said sustained-release preparation can reduce toxic reaction, at the same time can increase selectively drug concentration, and enhance therapeutic effectiveness.

L33 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1221757 CAPLUS
DOCUMENT NUMBER: 146:50223
TITLE: Sustained-release microsphere injection formulations of angiogenesis inhibitors combination with phosphoinositide-3-kinase inhibitor, pyrimidine analog, and DNA repairase inhibitor for cancer therapy
INVENTOR(S): Sun, Zhongxian
PATENT ASSIGNEE(S): Jinan Shuaihua Pharmaceutical Science and Technology

Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 34pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1861047	A	20061115	CN 2006-10200196	20060306

PRIORITY APPLN. INFO.: CN 2006-10200196 20060306

AB The invention provides sustained-release microsphere injection formulations of angiogenesis inhibitors combination with phosphoinositide-3-kinase inhibitor, pyrimidine analog, and DNA repairase inhibitor for cancer therapy. The antitumor sustained-release injection is comprised of (A) sustained-release microsphere comprising antitumor effective constituent 0.5-60 wt%, and sustained-release adjuvant 40-99 wt%, and suspending agent 0.0-30 wt%; and (B) solvent. The antitumor effective constituent is vascular inhibitor and its synergistic agent from phosphoinositide-3-kinase inhibitor, pyrimidine analog, and/or DNA repairase inhibitor. The vascular inhibitor is selected form one of gefitinib, tarceva, lapatinib, angiostatin, avastin, canertinib, panitumumab, or the mixture thereof. The phosphoinositide-3-kinase inhibitor is selected from one of 7-hydroxyl-staurosporine, 7-oxy-alkyl-staurosporine, β-methoxyl staurosporine, etc., or the mixture thereof. The pyrimidine analog is selected from one of 04-benzyl folic acid, 2,4,5-triamino-6-benzyloxy pyrimidine, 2,4-diamino-6-benzyloxy-5-nitrosopyrimidine, 2-amino-O-4-benzyl pteridine, etc., or the mixture thereof. The DNA repairase inhibitor is selected from one of (a) 2-(morphol-4-yl)-benzo[h]chromone-4-one, 2-(4-morpholinyl)-8-Ph chromone, etc.; (b) 3-aminobenzamide, benzamide, 3,4-dihydro methoxyisoquinolin-1(2H)-benzamide, etc.; and (c) aminotriazole, DL-buthionine(S,R)-sulfoximine, calvatic acid, S-hexyl glutathione, etc. The sustained-release adjuvant is selected from one of (a) polylactic acid; (b) Polyglycolic acid-hydroxy acetic acid copolymer; (c) polifeprosan; (d) ethene-vinyl acetate copolymer; (e) difatty acid-sebacic acid copolymer; (f) poly(erucic acid dimer-sebacic acid) copolymer; (g) poly(fumaric acid-sebacic acid) copolymer; (h) sodium CM-cellulose, hydroxypropyl cellulose, xylitol, oligosaccharide, chondroitin, chitin, hyaluronic acid, collagens, etc.; or (i) racemic polylactic acid, etc., or the mixture thereof. The suspending agent is one of (a) 0.5-3.0 % (sodium) CM-cellulose; (b) 5-15 % mannitol; (c) 5-15 % sorbitol; (d) 0.1-1.5 % surfactant; (e) 0.1-0.5 % tween 20; (f) (iodine) glycerin, dimethicone, propylene glycol, or carbomer; (g) 0.5-5 % sodium CM-cellulose + 0.1-0.5 % tween 80; (h) 5-20 % mannitol + 0.1-0.5 % tween 80; or (i) 0.5-5 % sodium CM-cellulose + 5-20 % sorbitol + 0.1-0.5 % tween 80. The sustained-release preparation can reduce toxic reaction, at the same time can increase selectively drug concentration, and enhance therapeutic effectiveness.

L33 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1202128 CAPLUS
DOCUMENT NUMBER: 146:13110
TITLE: Antitumor sustained-release injection containing anti-metabolic antitumor drug and/or its synergistic agent from alkylating agent and/or guanine analogs
INVENTOR(S): Kong, Qingzhong; Sun, Juan; Zhang, Hongjun; Chen, Ying
PATENT ASSIGNEE(S): Shandong Lan-Jin Bioengineering Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 31pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1857209	A	20061108	CN 2006-10200258	20060317
PRIORITY APPLN. INFO.:			CN 2006-10200258	20060317

AB The sustained-release injection is comprised of (A) sustained-release microsphere comprising antitumor effective constituent 0.5-60, sustained-release adjuvant 40-99 wt% and suspending agent 0.0-30 wt%; and (B) solvent. The antitumor effective constituent is selected from anti-metabolic antitumor drug and/or its synergistic agent which is alkylating agent and/or purine analogs. The anti-metabolic antitumor drugs are selected from alimta, alimta disodium, carmofur, tegafur, zalcitabine, etc. The guanine analogs are selected from, O6-benzyl guanine, O6-Bu guanine, O6-Me guanine, O6-alkyl guanine, O6-benzyl uric acid or O6-benzyl xanthine.
The alkylating agent is selected from one of ambamustine, nimustine, bendamustine, lomustine, tallimustine, melphalan, etc., or the mixture thereof. The sustained-release adjuvant is selected from one of a) polylactic acid; b) Polyglycolic acid-hydroxy acetic acid copolymer; c) polifeprosan; d) ethene-vinyl acetate copolymer; e) difatty acid-sebacic acid copolymer; f) poly(erucic acid dimer-sebacic acid) copolymer; g) poly(fumaric acid-sebacic acid) copolymer; h) sodium CM-cellulose, hydroxypropyl cellulose, xylitol, oligosaccharide, chondroitin, chitin, hyaluronic acid, collagens, etc.; or the mixture thereof.
The suspending agent is one of a) 0.5-3.0 % (sodium) CM-cellulose; b) 5-15 % mannitol; c) 5-15 % sorbitol; d) 0.1-1.5 % surfactant; e) 0.1-0.5 % tween 20; f) (iodine) glycerin, dimethicone, propylene glycol, or carbomer; g) 0.5-5 % sodium CM-cellulose + 0.1-0.5 % tween 80; h) 5-20 % mannitol + 0.1-0.5 % tween 80; or i) 0.5-5 % sodium CM-cellulose + 5-20 % sorbitol + 0.1-0.5 % tween 80.

L35 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:289133 CAPLUS
DOCUMENT NUMBER: 125:6909
TITLE: Inter-α-trypsin inhibitor bound to tumor cells is cleaved into the heavy chains and the light chain on the cell surface
AUTHOR(S): Kobayashi, Hiroshi; Gotoh, Junko; Hirashima, Yasuyuki; Terao, Toshihiko
CORPORATE SOURCE: Dep. Obstetrics Gynecology, Hamamatsu Univ. School Medicine, Hamamatsu, 431-31, Japan
SOURCE: Journal of Biological Chemistry (1996), 271(19), 11362-11367
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Inter-α-trypsin inhibitor (ITI), a human serum protease inhibitor of mol. mass 240 kDa which may release physiol. derivs., has been shown to interact with hyaluronic acid (HA), resulting in pericellular matrix stabilization (Chen, L., Mao, S. J. T., McLean, L. R., Powers, R. W., and Larsen, W. J. (1994) J. BIol. CHem. 269, 28282-28287). The purpose of this study is to determine whether ITI binding to tumor cell surface is mediated by urinary trypsin inhibitor (UTI) receptor or cell-associated hyaluronic acid (HA). We demonstrated specific complex formation of the heavy (H) chains of ITI with HA. Binding of the H-chains of ITI to immobilized HA was detected and quantified using colorimetric immunoassays. Binding was time-, temperature-, and concentration-dependent. However, UTI and HI-8 (the carboxyl terminus of UTI) failed to bind to immobilized HA. ITI bound to HA retained functional protease inhibiting activity. After incubation of SMT-cc1 cells with purified biotinylated ITI, biotinylated ITI is bound to the cells, dissociated, and gives rise to the H-chains and UTI on the cell surface. The cell surface receptor-bound UTI derived from ITI may be the result of the limited proteolysis on the cell surface. In the cells treated with hyaluronidase, bound H-chains disappeared from the surface of the cells, while most of the cell surface ITI derivs. was present in deglycosylated UTI (28 kDa). It is suggested that the binding of ITI to the cell surface is mediated by HA on the cells. This was confirmed by the fact that the hyaluronidase-treated cells can abolish the ITI binding. The cell surface UTI formation was inhibited by diisopropyl fluorophosphate, phenylmethylsulfonyl fluoride, and eglin C, suggesting that elastase-like enzyme(s) may be responsible for the UTI formation. Preincubation of the cells with UTI did not decrease in exogenously added ITI on the cell surface. A model for cell surface UTI formation is proposed in which ITI binding to cells from serum used for the culture is followed by the limited proteolysis by trace amts. of active serine proteases, to form cell-surface receptor-bound UTI and the H-chains intercalated into cell surface HA. This process is subject to regulation of cell-associated UTI and of stabilization of pericellular matrix.

L35 ANSWER 2 OF 3 MEDLINE on STN
ACCESSION NUMBER: 96212206 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8626690
TITLE: Inter-alpha-trypsin inhibitor bound to tumor cells is cleaved into the heavy chains and the light chain on the cell surface.
AUTHOR: Kobayashi H; Gotoh J; Hirashima Y; Terao T
CORPORATE SOURCE: Department of Obstetrics and Gynecology, Hamamatsu University School of Medicine, Shizuoka, Japan.
SOURCE: The Journal of biological chemistry, (1996 May 10) Vol. 271, No. 19, pp. 11362-7.

Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199606
ENTRY DATE: Entered STN: 8 Jul 1996
Last Updated on STN: 6 Feb 1998
Entered Medline: 27 Jun 1996

AB Inter-alpha-trypsin inhibitor (ITI), a human serum protease inhibitor of molecular mass 240 kDa which may release physiological derivatives, has been shown to interact with hyaluronic acid (HA), resulting in pericellular matrix stabilization (Chen, L., Mao, S.J.T., McLean, L. R., Powers, R. W., and Larsen, W. J. (1994) J. Biol. Chemical 269, 28282-28287). The purpose of this study is to determine whether ITI binding to tumor cell surface is mediated by urinary trypsin inhibitor (UTI)-receptor or cell-associated hyaluronic acid (HA). We demonstrated specific complex formation of the heavy (H) chains of ITI with HA. Binding of the H-chains of ITI to immobilized HA was detected and quantified using colorimetric immunoassays. Binding was time-, temperature-, and concentration-dependent. However, UTI and HI-8 (the carboxyl terminus of UTI) failed to bind to immobilized HA. ITI bound to HA remained functional protease inhibiting activity. After incubation of SMT-cc1 cells with purified biotinylated ITI, biotinylated ITI is bound to the cells, dissociated, and gives rise to the H-chains and UTI on the cell surface. The cell surface receptor-bound UTI derived from ITI may be the result of the limited proteolysis on the cell surface. In the cells treated with hyaluronidase, bound H-chains disappeared from the surface of the cells, while most of the cell surface ITI derivatives was present in deglycosylated UTI (28 kDa). It is suggested that the binding of ITI to the cell surface is mediated by HA on the cells. This was confirmed by the fact that the hyaluronidase-treated cells can abolish the ITI binding. The cell surface UTI formation was inhibited by diisopropyl fluorophosphate, phenylmethylsulfonyl fluoride, and eglin C, suggesting that elastase-like enzyme(s) may be responsible for the UTI formation. Preincubation of the cells with UTI did not decrease in exogenously added ITI on the cell surface. A model for cell surface UTI formation is proposed in which ITI binding to cells from serum used for the culture is followed by the limited proteolysis by trace amounts of active serine proteases, to form cell-surface receptor-bound UTI and the H-chains intercalated into cell surface HA. This process is subject to regulation of cell-associated UTI and of stabilization of pericellular matrix.

L35 ANSWER 3 OF 3 MEDLINE on STN
ACCESSION NUMBER: 87109487 MEDLINE
DOCUMENT NUMBER: PubMed ID: 3805131
TITLE: Murine macrophage heparanase: inhibition and comparison with metastatic tumor cells.
AUTHOR: Savion N; Disatnik M H; Nevo Z
SOURCE: Journal of cellular physiology, (1987 Jan) Vol. 130, No. 1, pp. 77-84.
Journal code: 0050222. ISSN: 0021-9541.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198703
ENTRY DATE: Entered STN: 3 Mar 1990
Last Updated on STN: 3 Feb 1997
Entered Medline: 11 Mar 1987

AB Circulating macrophages and metastatic tumor cells can penetrate the vascular endothelium and migrate from the circulatory system to

extravascular compartments. Both activated murine macrophages and different metastatic tumor cells (B16-BL6 melanoma; ESb T-lymphoma) attach, invade, and penetrate confluent vascular endothelial cell monlayer in vitro, by degrading heparan sulfate proteoglycans in the subendothelial extracellular matrix. The sensitivity of the enzymes from the various sources degrading the heparan sulfate proteoglycan was challenged and compared by a series of inhibitors. Activated macrophages demonstrate a heparanase with an endoglycosidase activity that cleaves from the [35S]O4 = -labeled heparan sulfate proteoglycans of the extracellular matrix 10 kDa glycosaminoglycan fragments. The macrophages do not store the heparanase intracellularly but it is instead found pericellularly and requires a continuous cell-matrix contact at the optimal pH for maintaining cell growth. The degradation of [35S]O4 = -labeled extracellular matrix proteoglycans by the macrophages' heparanase is significantly inhibited in the presence of heparan sulfate (10 micrograms/ml), arteparon (10 micrograms/ml), and heparin at a concentration of 3 micrograms/ml. In contrast, other glycosaminoglycans such as hyaluronic acid, dermatan sulfate, and chondroitin sulfate as well as the specific inhibitor of exo-beta-glucuronidase D-saccharic acid 1,4-lactone failed to inhibit the degradation of sulfated proteoglycans in the subendothelial extracellular matrix. Degradation of this heparan sulfate proteoglycan is a two-step sequential process involving protease activity followed by heparanase activity. However, the following antiproteases--alpha 2-macroglobulin, antithrombin III, leupeptin, and phenylmethylsulfony fluoride (PMSF)--failed to inhibit this degradation process, and only alpha 1-antitrypsin inhibited the heparanase activity. B16-BL6 metastatic melanoma cell heparanase, which is also a cell-associated enzyme, was inhibited by heparin to the same extent as the macrophage heparanase. On the other hand, heparanase of the highly metastatic variant (ESb) of a methylcholanthrene-induced T lymphoma, which is an extracellular enzyme released by the cells to the incubation medium, was more sensitive to heparin and arteparon than the macrophages' heparanase, inhibited at concentrations of 1 and 3 micrograms/ml, respectively. These results may indicate the potential use of heparin or other glycosaminoglycans as specific and differential inhibitors for the formation in certain cases of blood-borne tumor metastasis.

L37 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:694981 CAPLUS
DOCUMENT NUMBER: 143:482971
TITLE: Implantation of preadipocyte-loaded hyaluronic acid-based scaffolds into nude mice to evaluate potential for soft tissue engineering
AUTHOR(S): Hemmrich, Karsten; von Heimburg, Dennis; Rendchen, Raoul; Di Bartolo, Chiara; Milella, Eva; Pallua, Norbert
CORPORATE SOURCE: Department of Plastic Surgery and Hand Surgery, University Hospital of the Aachen University of Technology, Aachen, D-52057, Germany
SOURCE: Biomaterials (2005), 26(34), 7025-7037
CODEN: BIMADU; ISSN: 0142-9612
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The reconstruction of soft tissue defects following extensive deep burns or tumor resections remains an unresolved problem in plastic and reconstructive surgery since adequate implant materials are still not available. Preadipocytes, immature precursor cells found between mature adipocytes in adipose tissue, are a potential material for soft tissue engineering since they can proliferate and differentiate into adipose tissue after transplantation. In previous studies, the authors identified hyaluronan benzyl ester (HYAFF-11) sponges to be promising carrier matrixes. This study now evaluates, in vitro and in vivo, a new sponge architecture with pores of 400 μm either made of plain HYAFF-11 or HYAFF-11 coated with the extracellular matrix glycosaminoglycan hyaluronic acid. Human preadipocytes were isolated, seeded onto carriers and implanted into nude athymic mice. Explants harvested after 3, 8, and 12 wk were examined for macroscopical appearance, thickness, weight, pore structure, histol., and immunohistochem. Compared to previous studies, the authors found better penetration of cells into both types of scaffolds, with more extensive formation of new vessels throughout the construct but with only minor adipose tissue. The authors' encouraging results contribute towards a better seeded and vascularized scaffold but also show that the enhancement of adipogenic conversion of preadipocytes remains a major task for further in vivo expts.
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L37 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:591962 CAPLUS
DOCUMENT NUMBER: 143:91004
TITLE: Use of PSP64 and subfragments to suppress cell adhesion and migration, inhibit matrix metalloproteinase secretion, and treat cancer and other diseases
INVENTOR(S): Panchal, Chandra J.; Wu, Jinzi Jason; Beliveau, Richard; Ruiz, Marcia; Garde, Seema; Annabi, Borhane; Lamy, Sylvie; Bouzeghrane, Mounia; Daigneault, Luc; Hawkins, Robert
PATENT ASSIGNEE(S): Can.
SOURCE: U.S. Pat. Appl. Publ., 59 pp., Cont.-in-part of U.S. Ser. No. 948,229.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 5
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 2005147601	A1	20050707	US 2004-4270		20041202
CA 2441695	A1	20050326	CA 2003-2441695		20030926
US 2005096273	A1	20050505	US 2004-948229		20040924
AU 2005250059	A1	20051215	AU 2005-250059		20050321
CA 2567901	A1	20051215	CA 2005-2567901		20050321
WO 2005118623	A1	20051215	WO 2005-CA430		20050321

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1765852	A1	20070328	EP 2005-714663	20050321

R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, AL, BA, HR, LV, MK, YU

PRIORITY APPLN. INFO.:

CA 2003-2441695	A	20030926
US 2004-948229	A2	20040924
US 2004-857358	A	20040601
US 2004-4270	A	20041202
US 2004-4273	A	20041202
WO 2005-CA430	W	20050321

AB Matrix metalloproteinases (MMPs) play an important role in morphogenesis, angiogenesis, wound healing, and in certain disorders such as rheumatoid arthritis, tumor invasion and metastasis. MMPs are thought to be regulated by a variety of cytokines, growth factors, hormones and phorbol esters. This regulation occurs on three levels; alteration of gene expression, activation of the latent zymogen and inhibition by the tissue inhibitors of metalloproteinases (TIMP). We report here a new agent that regulates the level of MMPs, i.e., prostate secretory protein PSP94. Thus, PCK3145, a pentadecapeptide derived from PSP94, significantly decreased levels of MMP-9 in the blood of patients with metastatic adenocarcinoma of the prostate. A derivative of PCK3145 in which the 3 cysteine SH groups were acetaminomethylated, suppressed secretion of MMP from Mat-LyLu cells. This derivs. also decreased U-87 cell adhesion to hyaluronic acid as well as U-87 cell migration. Further effects of the PSP94 peptide derivative were increased CD44 cell surface shedding and induction of RhoA protein expression.

L37 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2003:551368 CAPLUS
DOCUMENT NUMBER: 139:122818
TITLE: Biomaterials based on hyaluronic acid for the anti-angiogenic therapy in the treatment of tumors
INVENTOR(S): Fusenig, Norbert E.; Stark, Hans-Juergen; Willhauck, Michael; Pavesio, Alessandra
PATENT ASSIGNEE(S): Fidia Farmaceutici S.p.A., Italy; Deutsches Krebsforschungszentrum (DKFZ)
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003057203	A2	20030717	WO 2003-EP78	20030107
WO 2003057203	A3	20031231		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

IT 2002PD0003	A1	20030711	IT 2002-PD3	20020111
CA 2472880	A1	20030717	CA 2003-2472880	20030107
AU 2003201618	A1	20030724	AU 2003-201618	20030107
EP 1463541	A2	20041006	EP 2003-700315	20030107

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

JP 2005524619	T	20050818	JP 2003-557561	20030107
US 2005037049	A1	20050217	US 2004-501030	20040812

PRIORITY APPLN. INFO.:	IT 2002-PD3	A	20020111
	WO 2003-EP78	W	20030107

AB The use in the medical-surgical field of biomaterials based on hyaluronic acid derivs., optionally in association with natural, synthetic or semi-synthetic biopolymers, for suppressing the angiogenic process associated with tumor proliferation (in primary and secondary tumors) is disclosed. For example, the Hyaff 11-based biomaterial proved able to modulate/inhibit the angiogenic process related to vascularization of the cancerous epithelium.

L37 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2003:286155 CAPLUS
DOCUMENT NUMBER:	139:211727
TITLE:	Influences of hyaluronic acid binding protein on expressions of human cancer cells cyclin E and p27kip1
AUTHOR(S):	Gao, Feng; Sun, Tinglu; Cao, Manlin; Zhang, Lurong; Underhill, C. B.
CORPORATE SOURCE:	Department of Clinical Laboratory, Shanghai Sixth People's Hospital, Shanghai, 200233, Peop. Rep. China
SOURCE:	Shanghai Yixue (2002), 25(9), 581-583 CODEN: SIHSD8; ISSN: 0253-9934
PUBLISHER:	Shanghai Yixue Bianji Weiyuanhui
DOCUMENT TYPE:	Journal
LANGUAGE:	Chinese

AB The influences of hyaluronic acid binding protein (HABP) on expressions of human cancer cells cyclin E and p27kip1 and adult bovine arterial endothelial cells (ABAE) p27kip1 were studied. Full length cDNA of human brain hyaluronic acid binding protein (hbHABP) was transfected into human breast cancer cell line (MDA435) and prostatic cancer cell line (TSU). Cyclin E and p27kip1 expression from these transfectants were detected by Western blot. In addition, conditioned medium (CM) from these transfectants was added to the cultured ABAE, and the p27kip1 expression was also determined The expression of cyclin E was decreased and that of p27kip1 was markedly increased in both MDA435 and TSU cells. There expression of p27kip1 in ABAE cells was increased in the presence of the CM. The hbHABP may have the inhibitory effects on human breast cancer and prostate cancer cells growth via the following mechanisms: from inhibiting cancer cells cyclin E expression and inducing inhibitor of cyclin-dependent kinase p27kip1 expression, inhibiting tumor angiogenesis by increasing endothelial cells p27kip1 expression.

L37 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER:	2002:251037 CAPLUS
DOCUMENT NUMBER:	137:214497
TITLE:	Promotion of growth of human breast cancer cells

MDA231 by human sperm membrane-bound hyaluronidase
AUTHOR(S): Gao, Feng; Zhang, Lurong; Charles, B. Underhill
CORPORATE SOURCE: Department of Clinical Laboratory, Shanghai No.6 People's Hospital, Shanghai, 200233, Peop. Rep. China
SOURCE: Zhonghua Yixue Zazhi (Beijing, China) (2002), 82(3), 207-210
CODEN: CHHTAT; ISSN: 0376-2491
PUBLISHER: Zhonghua Yixue Zazhishe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The mechanism how human sperm membrane-bound hyaluronidase promotes the growth of human breast cancer was studied. Full-length cDNA of human PH20 was transfected into human breast cancer cell line MDA231. The transfectant MDA231-PH20 was then implanted into the chorioallantoic membrane (CAM) of chicken embryo to form a tumor. Four days after implantation, the tumors were resected and weighted. The angiogenesis in tumor tissue was examined by immunohistochem. Trans-well cell culture was used to study the effect of MDA231-PH20 on the growth of adult bovine aortic endothelial cells . The expression of fibroblast growth factor-2 (FGF-2) in the tumor cells was investigated by Western blotting. ELISA was used to examine the secretion of FGF-2 and hyaluronic acid.
The same amount of blank vector pcDNA3, instead of PH20, was transfected into human breast cancer cell line MDA231 as control group. The average weight of tumor four days after implantation was 44.7 mg±10.2 mg in the MDA231-Ph20 group, and was 21.3 gm±2.8 mg in the control group. Neogenetic vessels increased remarkably in MDA231-PH20 tumor tissues. The expression of FGF-2 protein was much higher in MDA231-PH20 cells. The FGF content and HA secretion were higher in the MDA231-PH20 group than in the control group. The growth of ABAE cells was significantly accelerated after co-culture with MDA231-PH20 transfectant. PH20 may promote the growth of human breast cancer by accelerating the release of FGF-2 from tumor cells, decomposing HA into small fragments, and promoting angiogenesis.

L37 ANSWER 6 OF 6 MEDLINE on STN
ACCESSION NUMBER: 2002217451 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11953163
TITLE: Promotion of growth of human breast cancer cells MDA231 by human sperm membrane-bound hyaluronidase: an experimental study.
AUTHOR: Gao Feng; Zhang Lurong; Underhill Charles B
CORPORATE SOURCE: Department of Clinical Laboratory, Shanghai No. 6 People's Hospital, Shanghai 200233, China.
SOURCE: Zhonghua yi xue za zhi, (2002 Feb 10) Vol. 82, No. 3, pp. 207-10.
Journal code: 7511141. ISSN: 0376-2491.
PUB. COUNTRY: China
DOCUMENT TYPE: (ENGLISH ABSTRACT)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200207
ENTRY DATE: Entered STN: 16 Apr 2002
Last Updated on STN: 3 Jul 2002
Entered Medline: 2 Jul 2002

AB OBJECTIVE: To study the mechanism how human sperm membrane-bound hyaluronidase (PH20) promotes the gowth of human breast cancer. METHODS: Full-length cDNA of human PH20 was transfected into human breast cancer cell line MDA231. The transfectant MDA231-PH20 was then implanted into the chorio-allantoic membrane (CAM) of chicken embryo to form a tumor. Four days after implantation, the tumors were resected to be weighed. The angiogenesis in tumor tissue was examined by immunohistochemistry. Trans-well cell culture was

used to study the effect of MDA231-PH20 on the growth of adult bovine aortic endothelial cells (ABAE). The expression of fibroblast growth factor-2 (FGF-2) in the tumor cells was investigated by Western blotting. ELISA was used to examine the secretion of FGF-2 and hyaluronic acid. The same amount of empty vector pcDNA3, instead of PH20, was transfected into human breast cancer cell line MDA231 as control group. RESULTS: The average weight of tumor four days after implantation was 44.7 mg +/- 10.2 mg in the MDA231-PH20 group, and was 21.3 mg +/- 2.8 mg in the control group ($t = 2.418$, $P = 0.038$). Neogenetic vessels increased remarkably in MDA231-PH20 tumor tissues. The expression of FGF-2 protein was much higher in MDA231-PH20 cells. The FGF content and HA secretion were higher in the MDA231-PH20 group than in the control group (8.10 pg/ml +/- 1.56 pg/ml vs. 3.94 pg/ml +/- 0.82 pg/ml, and 1 220 ng/ml +/- 254 ng/ml vs. 462 ng/ml +/- 96 ng/ml, all $P < 0.01$). The growth of ABAE cells was significantly accelerated after co-culture with MDA231-PH20 transfectant. CONCLUSION: PH20 may promote the growth of human breast cancer by accelerating the release of FGF-2 from tumor cells, decomposing HA into small fragments, and promoting angiogenesis.

L38 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:694981 CAPLUS
DOCUMENT NUMBER: 143:482971
TITLE: Implantation of preadipocyte-loaded hyaluronic acid-based scaffolds into nude mice to evaluate potential for soft tissue engineering
AUTHOR(S): Hemmrich, Karsten; von Heimburg, Dennis; Rendchen, Raoul; Di Bartolo, Chiara; Milella, Eva; Pallua, Norbert
CORPORATE SOURCE: Department of Plastic Surgery and Hand Surgery, University Hospital of the Aachen University of Technology, Aachen, D-52057, Germany
SOURCE: Biomaterials (2005), 26(34), 7025-7037
CODEN: BIMADU; ISSN: 0142-9612
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The reconstruction of soft tissue defects following extensive deep burns or tumor resections remains an unresolved problem in plastic and reconstructive surgery since adequate implant materials are still not available. Preadipocytes, immature precursor cells found between mature adipocytes in adipose tissue, are a potential material for soft tissue engineering since they can proliferate and differentiate into adipose tissue after transplantation. In previous studies, the authors identified hyaluronan benzyl ester (HYAFF-11) sponges to be promising carrier matrixes. This study now evaluates, in vitro and in vivo, a new sponge architecture with pores of 400 μm either made of plain HYAFF-11 or HYAFF-11 coated with the extracellular matrix glycosaminoglycan hyaluronic acid. Human preadipocytes were isolated, seeded onto carriers and implanted into nude athymic mice. Explants harvested after 3, 8, and 12 wk were examined for macroscopical appearance, thickness, weight, pore structure, histol., and immunohistochem. Compared to previous studies, the authors found better penetration of cells into both types of scaffolds, with more extensive formation of new vessels throughout the construct but with only minor adipose tissue. The authors' encouraging results contribute towards a better seeded and vascularized scaffold but also show that the enhancement of adipogenic conversion of preadipocytes remains a major task for further in vivo expts.
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L38 ANSWER 2 OF 2 MEDLINE on STN
ACCESSION NUMBER: 2005400405 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15964623
TITLE: Implantation of preadipocyte-loaded hyaluronic acid-based scaffolds into nude mice to evaluate potential for soft tissue engineering.
AUTHOR: Hemmrich Karsten; von Heimburg Dennis; Rendchen Raoul; Di Bartolo Chiara; Milella Eva; Pallua Norbert
CORPORATE SOURCE: Department of Plastic Surgery and Hand Surgery, Burn Centre, University Hospital of the Aachen University of Technology, Germany.
SOURCE: Biomaterials, (2005 Dec) Vol. 26, No. 34, pp. 7025-37.
Journal code: 8100316. ISSN: 0142-9612.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: (EVALUATION STUDIES)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200512
ENTRY DATE: Entered STN: 3 Aug 2005
Last Updated on STN: 15 Dec 2005

Entered Medline: 7 Dec 2005

AB The reconstruction of soft tissue defects following extensive deep burns or tumor resections remains an unresolved problem in plastic and reconstructive surgery since adequate implant materials are still not available. Preadipocytes, immature precursor cells found between mature adipocytes in adipose tissue, are a potential material for soft tissue engineering since they can proliferate and differentiate into adipose tissue after transplantation. In previous studies, we identified hyaluronan benzyl ester (HYAFF 11) sponges to be promising carrier matrices. This study now evaluates, in vitro and in vivo, a new sponge architecture with pores of 400 microm either made of plain HYAFF 11 or HYAFF 11 coated with the extracellular matrix glycosaminoglycan hyaluronic acid. Human preadipocytes were isolated, seeded onto carriers and implanted into nude athymic mice. Explants harvested after 3, 8, and 12 weeks were examined for macroscopical appearance, thickness, weight, pore structure, histology, and immunohistochemistry. Compared to previous studies, we found better penetration of cells into both types of scaffolds, with more extensive formation of new vessels throughout the construct but with only minor adipose tissue. Our encouraging results contribute towards a better seeded and vascularised scaffold but also show that the enhancement of adipogenic conversion of preadipocytes remains a major task for further in vivo experiments.

L42 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:551368 CAPLUS
DOCUMENT NUMBER: 139:122818
TITLE: Biomaterials based on hyaluronic acid for the anti-angiogenic therapy in the treatment of tumors
INVENTOR(S): Fusenig, Norbert E.; Stark, Hans-Juergen; Willhauck, Michael; Pavesio, Alessandra
PATENT ASSIGNEE(S): Fidia Farmaceutici S.p.A., Italy; Deutsches Krebsforschungszentrum (DKFZ)
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003057203	A2	20030717	WO 2003-EP78	20030107
WO 2003057203	A3	20031231		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IT 2002PD0003	A1	20030711	IT 2002-PD3	20020111
CA 2472880	A1	20030717	CA 2003-2472880	20030107
AU 2003201618	A1	20030724	AU 2003-201618	20030107
EP 1463541	A2	20041006	EP 2003-700315	20030107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005524619	T	20050818	JP 2003-557561	20030107
US 2005037049	A1	20050217	US 2004-501030	20040812

PRIORITY APPLN. INFO.: IT 2002-PD3 A 20020111
WO 2003-EP78 W 20030107

AB The use in the medical-surgical field of biomaterials based on hyaluronic acid derivs., optionally in association with natural, synthetic or semi-synthetic biopolymers, for suppressing the angiogenic process associated with tumor proliferation (in primary and secondary tumors) is disclosed. For example, the Hyaff 11-based biomaterial proved able to modulate/inhibit the angiogenic process related to vascularization of the cancerous epithelium.

L42 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:9665 CAPLUS
DOCUMENT NUMBER: 139:138665
TITLE: Hyaluronan scaffolds for adipose tissue reconstruction
AUTHOR(S): von Heimburg, D.; Pallua, N.
CORPORATE SOURCE: Department of Plastic Surgery and Hand Surgery - Burn Centre, University Hospital of the Aachen University of Technology, Aachen, 52057, Germany
SOURCE: Hyaluronan, [Proceedings of the International Cellucon Conference], 12th, Wrexham, United Kingdom, 2000 (2002), Meeting Date 2000, Volume 2, 99-108. Editor(s): Kennedy, John F. Woodhead Publishing Ltd.: Cambridge, UK.
CODEN: 69DKVZ; ISBN: 1-85573-570-9
DOCUMENT TYPE: Conference
LANGUAGE: English

AB To date no adequate implant material for the correction of soft tissue defects such as after extensive deep burns, after tumor resection and in hereditary and congenital defects is available. A biohybrid composed of viable adipocyte-precursor cells and an optimized matrix could help towards a solution After being grafted preadipocytes demand an environment to differentiate into mature adipocytes (cell diameter up to 120 μm). Hyaluronan matrixes seeded with dedifferentiated preadipocytes were evaluated in the immunodeficient mouse model. Isolated and cultured human preadipocytes were seeded onto hyaluronan scaffolds (HYAFF 11 sponges, HYAFF 11 non-woven carrier and ACP sponges) sized 7.5 x 7.5 x 5 mm and implanted into 42 immunodeficient mice. The transplanted scaffolds without cells were used in the controls. After 3 and 8 wk (2 and 4 wk in ACP) the grafts were excised. Macroscopical impression, weight, thickness, histol., immunohistochem. (scaffold structure, cellularity, penetration depth of the seeded cells) and ultrastructure were assessed after 24 h in vitro and after explantation at 3 and 8 wk. Macroscopically after 3 and 8 wk in vivo layers of adipose tissue accompanied by new vessels were found in all HYAFF 11 preadipocyte/hyaluronan carriers. The control grafts appeared unchanged without vessel ingrowth. The ACP sponges were only present after two weeks of implantation, after four weeks ACP carriers were not present. The histol. of the preadipocyte/hyluronan carriers showed adipose tissue and a rich vascularization in the upper layers of the grafts, there was no homogeneous vessel distribution. The controls contained only few cells and a capsule but no adipose tissue. Human-vimentin pos. cells were found in all preadipocyte/hyaluronan grafts but not in the controls, penetrating maximum 2227μm±706μm (in sponges after 8 wk). Ultra-structural anal. showed complete in vivo differentiation of viable adipocytes in the sponge seeded with preadipocytes. The transplantation of isolated and cultured human preadipocytes within a standardized hyaluronan matrix resulted in well vascularized adipose-like tissue. It is assumed that the sponge structure is superior as preadipocytes enlarge during differentiation due to incorporation of lipids.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L43 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:551368 CAPLUS
DOCUMENT NUMBER: 139:122818
TITLE: Biomaterials based on hyaluronic acid for the anti-angiogenic therapy in the treatment of tumors
INVENTOR(S): Fusenig, Norbert E.; Stark, Hans-Juergen; Willhauck, Michael; Pavesio, Alessandra
PATENT ASSIGNEE(S): Fidia Farmaceutici S.p.A., Italy; Deutsches Krebsforschungszentrum (DKFZ)
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003057203	A2	20030717	WO 2003-EP78	20030107
WO 2003057203	A3	20031231		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
IT 2002PD0003	A1	20030711	IT 2002-PD3	20020111
CA 2472880	A1	20030717	CA 2003-2472880	20030107
AU 2003201618	A1	20030724	AU 2003-201618	20030107
EP 1463541	A2	20041006	EP 2003-700315	20030107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005524619	T	20050818	JP 2003-557561	20030107
US 2005037049	A1	20050217	US 2004-501030	20040812

PRIORITY APPLN. INFO.:
IT 2002-PD3 A 20020111
WO 2003-EP78 W 20030107

AB The use in the medical-surgical field of biomaterials based on hyaluronic acid derivs., optionally in association with natural, synthetic or semi-synthetic biopolymers, for suppressing the angiogenic process associated with tumor proliferation (in primary and secondary tumors) is disclosed. For example, the Hyaff 11-based biomaterial proved able to modulate/inhibit the angiogenic process related to vascularization of the cancerous epithelium.

L46 ANSWER 8 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2002:792089 CAPLUS
DOCUMENT NUMBER: 137:299928
TITLE: Pharmaceutical formulation for the treatment of gynecological diseases
INVENTOR(S): Yui, Nobuhiko; Murakami, Kouichi; Ooya, Tooru; Sato, Ikuo
PATENT ASSIGNEE(S): Chisso Corp., Japan
SOURCE: Eur. Pat. Appl., 10 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1249247	A2	20021016	EP 2002-7213	20020327
EP 1249247	A3	20030115		
EP 1249247	B1	20070228		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2002356447	A	20021213	JP 2002-80018	20020322
US 2002150605	A1	20021017	US 2002-108298	20020328
US 7041310	B2	20060509		

PRIORITY APPLN. INFO.: JP 2001-100426 A 20010330
AB This invention provides to a novel pharmaceutical formulation for the treatment of gynecol. diseases. The formulation comprises a drug for the intrauterine, intravaginal or intrapelvic administration, or for the administration into the ovarian endometrioma, and a biodegradable polymer comprising a chemical modified hyaluronic acid or a salt thereof prepared by O-acylating, alkoxylating or crosslinking a complex of hyaluronic acid or a salt thereof and a cationic compound in a nonaq. solvent. The preparation of the invention is preferably administered intrauterine, intravaginal, intrapelvic, and intratumor cavity. A suspension of distearyldimethylammonium chloride (DSC) in water was added to a solution of sodium hyaluronate (CHA) in water and the solution and the suspension were heated up to 45°. The resultant complex was recovered by centrifuging at 5000 rpm at room temperature and washed with warm water at 45°. After washing, the complex was lyophilized overnight and further vacuum-dried at 50° to give a CHA-DSC complex.

L46 ANSWER 9 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2001:383876 CAPLUS
DOCUMENT NUMBER: 135:17466
TITLE: Differential expression of CD44 isoforms during liver regeneration in rats
AUTHOR(S): Della Fazia, Maria Agnese; Pettirossi, Valentina; Ayroldi, Emira; Riccardi, Carlo; Magni, Mariapia Viola; Servillo, Giuseppe
CORPORATE SOURCE: Dipartimento di Scienze Biochimiche e di Biotecnologie Molecolari, Sezione di Fisiopatologia, Universita di Perugia, Perugia, 06100, Italy
SOURCE: Journal of Hepatology (2001), 34(4), 555-561
CODEN: JOHEEC; ISSN: 0168-8278
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Antigen CD44 is a transmembrane glycoprotein known to bind hyaluronic acid (HA). This mol. is a multifunctional cell surface glycoprotein involved in lymphocyte homing and activation, tumor growth, and metastasis. Here, the authors investigated the

qual. modification of CD44 in the regenerating liver as a model for studying cellular proliferation in vivo. Mols. involved in cell adhesion and the extracellular matrix (ECM), which influence differentiation, growth, cell-cell interactions, and cellular polarity, play an important role in the liver regeneration. The authors studied the modulation of CD44 gene expression and its post-transcriptional modifications, analyzing the expression of different isoforms containing exon v6 in the regenerating liver, in sham-operated liver and in hepatoma H-35 cells. The expression of CD44 and CD44v6 were analyzed in RNA extracted from regenerating liver at different times after partial hepatectomy (PH), and in H-35 hepatoma cells by Northern blot, RT-PCR and Southern blot, and in protein exts. from regenerating liver by Western blot. H-35 hepatoma cells were assayed with the antibody crosslinked technique with CD44 antibodies. The standard CD44 form was expressed in regenerating liver and its levels were not modified following PH. However, the anal. revealed CD44 isoforms containing v6 in the 1st hours after PH as well as in the H-35 hepatoma cell line. H-35 cells treated with crosslinked anti-CD44 antibodies or HA showed an increased rate of incorporation of [3H]thymidine (30 and 25%, resp.) with respect to the control. These findings suggest that CD44 may play a role in the proliferation of residual hepatocytes following PH.

REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 10 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:574105 CAPLUS
DOCUMENT NUMBER: 133:183069
TITLE: Method for the controlled swelling of polymers in hydrophilic environment for the usage as hemostatic dressings
INVENTOR(S): Lahann, Joerg; Lendlein, Andreas
PATENT ASSIGNEE(S): Germany
SOURCE: Ger. Offen., 8 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19905796	A1	20000817	DE 1999-19905796	19990212
PRIORITY APPLN. INFO.:			DE 1999-19905796	19990212

AB The invention concerns a method for the controlled intracorporeal swelling of polymers that are prepared under hydrophobic conditions by crosslinking macromols. with chemical active bridging mols.; in the body, the bridging mols. are cleaved by enzymes when pH is altered using certain substances; as a result, the polymers are swelling. To maintain the acquired shape, another crosslinking is initiated by altering the pH to the original value. These polymers can be used as hemostatic dressings, blocking materials for arteries, tumors, etc. Macromols. are hydrogels e.g. polyacrylic acid, polymethacrylic acid, polyhydroxymethacrylate; or, polyelectrolytes and natural polymers, e.g. heparin, heparansulfate, hyaluronic acid.
Bridging mols. are amino acids, peptides, oligonucleotides, saccharides, terpenes, glucose amines, lipids, etc. Enzymes that cleave the bridging mols. in the body are e.g. trypsin, pepsin, renin; also stereo-selective enzymes can cleave. Various organs can be targetted, e.g. liver, kidney, pancreas, etc. To alter the pH, e.g. methylsulfonylethyl succinimidyl carbonate is reacted with hirudin.

L46 ANSWER 11 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1995:895402 CAPLUS
DOCUMENT NUMBER: 123:283157
TITLE: Involvement of CD44 variant isoforms in hyaluronate

adhesion by human activated T cells
AUTHOR(S): Galluzzo, Edi; Albi, Nicola; Fiorucci, Stefano; Merigiola, Carla; Ruggeri, Loredana; Tosti, Antonella; Grossi, Carlo E.; Velardi, Andrea
CORPORATE SOURCE: Dep. Clinical Medicine, Pathology and Pharmacology, Univ. Perugia, Perugia, Italy
SOURCE: European Journal of Immunology (1995), 25(10), 2932-9
CODEN: EJIMAF; ISSN: 0014-2980
PUBLISHER: VCH
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The standard, 85-94-kDa form of the hyaluronic acid (HA) receptor CD44 and a number of CD44 mRNA splice variants play important roles in immune responses and tumor metastasis. Variants carrying exon 6 (v6), or 9 (v9) products are transiently expressed on activated human T cells. Here, modulation expts. with specific monoclonal antibodies (mAb) indicate that v6 and v9 are expressed independently on distinct sets of CD44 mols., and that their combined expression is necessary for HA adhesion. Moreover, the finding that mAb-mediated crosslinking of v6 and v9 promoted cytosolic free Ca2+ mobilization and co-stimulated CD3-triggered T cell proliferation indicates that v6 and v9 possess signaling and effector function activation ability. Finally, HA-mediated signaling appears to be required for variant-dependent adhesion to HA. The observation that soluble HA promoted cytosolic free Ca2+ mobilization indicates that HA-induced Ca2+ mobilization can occur during T cell-HA interaction. Since Ca2+ mobilization was inhibited by pretreatment of cells with an anti-CD44 mAb directed against the HA-binding domain of CD44, CD44 receptors appear to be involved in HA-mediated signal transduction. The requirement of cytosolic free Ca2+ for adhesion is shown by the fact that ionomycin (a Ca2+ ionophore) stimulated, and EGTA (a Ca2+ chelator), inhibited HA adhesion. In addition, cytoskeletal activation is required for cell adhesion to HA, since drugs that block actin polymerization, such as cytochalasin B, or actomyosin contraction, such as the calmodulin antagonist W-7, inhibited cell adhesion to HA. As this adhesion is also ADP ribosylation-sensitive, it may involve a GTP-dependent function of CD44v, i.e. ankyrin binding. Thus, there is a functional hierarchy among the CD44 mols. expressed on human peripheral blood T cells and the splice variants, as compared to the standard form, exhibit a greater HA binding ability which involves CD44-mediated signaling and effector function activation.

L46 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1992:589900 CAPLUS
DOCUMENT NUMBER: 117:189900
TITLE: Stimulation of IFN-γ, TNF-α, and TNF-β secretion in IL-2-activated T cells: costimulatory roles for LFA-1, LFA-2, CD44, and CD45 molecules
AUTHOR(S): Chong, Anita S. F.; Boussy, Ian A.; Graf, Lloyd H.; Scuderi, Philip
CORPORATE SOURCE: Dep. Gen. Surg., Rush-Presbyterian-St. Luke's Med. Cent., Chicago, IL, 60612, USA
SOURCE: Cellular Immunology (1992), 144(1), 69-79
CODEN: CLIMB8; ISSN: 0008-8749
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Lymphokine-activated killer (LAK) cells are peripheral blood lymphocytes (PBLs) that possess the ability to kill target cells in a non-major histocompatibility complex (MHC)-restricted manner. Both NK and T cells can be stimulated with interleukin-2 (IL-2) to become LAK cells. Previously it was reported that the interaction of LAK cells with tumor cells also induces the secretion of interferon-γ (IFN-γ). The NK subset of LAK (LAK-NK) cells is stimulated by tumor cells to secrete IFN-γ in a non-MHC-restricted manner

while the T cell subset of LAK (LAK-T) cells is stimulated to secrete IFN-γ upon crosslinking of the T cell receptor (TCR)-CD3 complex. Here, LAK-T cells stimulated with anti-CD3 mAbs and tumor cells secrete two addnl. cytokines, tumor necrosis factor-α (TNF-α) and TNF-β/lymphotoxin (TNF-β). In addition, at least four other structurally unrelated mols. in addition to the TCR-CD3 complex, on LAK-T cells participate in the stimulation of IFN-γ, TNF-α, and TNF-β production These mols. are the lymphocyte function associated antigen-1 (LFA-1), lymphocyte function associated antigen-2 (LFA-2), CD44, and CD45. LFA-1 is an integrin, LFA-2 is a member of the Ig supergene family, CD44 is homologous to the cartilage link proteins, and CD45 is a tyrosine phosphatase. Ligands to three of these mols. have been identified; ICAM-1, LFA-3, and hyaluronic acid binding to LFA-1, LFA-2, and CD44, resp. LFA-1, LFA-2, and CD44 are reported to function both as adhesion mols. and as costimulators in resting T cells. The data suggest that these three mols. enhance IFN-γ, TNF-α, and TNF-β production by augmenting LAK-T cell to tumor cell adhesion and also by functioning as costimulators.

L46 ANSWER 13 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1986:142259 CAPLUS
DOCUMENT NUMBER: 104:142259
TITLE: Mucopolysaccharides as neoplasm inhibitors
INVENTOR(S): Sakurai, Katsukiyo; Horie, Katsuyuki; Sakamoto, Takashi; Okuyama, Takashi
PATENT ASSIGNEE(S): Seikagaku Kogyo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 61000017	A	19860106	JP 1984-118283	19840611
JP 04056805	B	19920909		

PRIORITY APPLN. INFO.: JP 1984-118283 19840611
AB Hyaluronic acid, crosslinked hyaluronic acid, and its salts are neoplasm inhibitors. Thus, hyaluronic acid (0.25 mg/mouse/day) in saline injected i.p. into mice bearing mammary gland tumor cells in blood prevented the metastasis of the tumor.

L46 ANSWER 14 OF 15 MEDLINE on STN
ACCESSION NUMBER: 2004532806 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15503629
TITLE: Anti-inflammatory drug delivery from hyaluronic acid hydrogels.
AUTHOR: Hahn Sei K; Jelacic Sandra; Maier Ronald V; Stayton Patrick S; Hoffman Allan S
CORPORATE SOURCE: Department of Bioengineering, University of Washington, Seattle, WA 98195, USA.. sekanhn@chugai-pharm.co.jp
CONTRACT NUMBER: R24 HL 64387 (NHLBI)
SOURCE: Journal of biomaterials science. Polymer edition, (2004) Vol. 15, No. 9, pp. 1111-9.
Journal code: 9007393. ISSN: 0920-5063.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: (IN VITRO)
Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
(RESEARCH SUPPORT, U.S. GOV'T, NON-P.H.S.)
(RESEARCH SUPPORT, U.S. GOV'T, P.H.S.)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200502
ENTRY DATE: Entered STN: 27 Oct 2004
Last Updated on STN: 16 Feb 2005
Entered Medline: 14 Feb 2005

AB Two different types of hyaluronic acid (HA) hydrogels were synthesized by crosslinking HA with divinyl sulfone (DVS) and poly(ethylene glycol)-divinyl sulfone (VS-PEG-VS). Vitamin E succinate (VES), an anti-inflammatory drug, and bovine serum albumin (BSA), a model of anti-inflammatory protein drugs, were loaded into the gels and their release kinetics were measured in vitro. VES and BSA released with a burst from both HA hydrogels during the first few hours, and release continued gradually for several days. The rate of release from HA-VS-PEG-VS-HA hydrogels was faster than that from HA-DVS-HA hydrogels, presumably due to the lower crosslink density in the former. The anti-inflammatory action of released VES was tested by incubating peripheral blood mononuclear cells (PBMC) on HA hydrogels with and without VES in the gel. The number of cells adhering on HA hydrogels was very low compared to that on tissue culture polystyrene (TCPS), which might be one of the important advantages of using HA hydrogels for implant coatings or tissue engineering applications. ELISA test results showed that the tumor necrosis factor-alpha (TNF-alpha) concentration was very low in the supernatant of the wells containing the HA hydrogel with VES in contact with the activated macrophages compared to that without VES. This is probably the effect of the released VES reducing the production of anti-inflammatory cytokine, TNF-alpha. HA hydrogels containing anti-inflammatory drugs may have potential for use in tissue engineering and also as biocompatible coatings of implants.

L46 ANSWER 15 OF 15 MEDLINE on STN
ACCESSION NUMBER: 1999186635 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10088774
TITLE: Synovial fluid transforming growth factor beta inhibits dendritic cell-T lymphocyte interactions in patients with chronic arthritis.
AUTHOR: Summers K L; O'Donnell J L; Heiser A; Highton J; Hart D N
CORPORATE SOURCE: Christchurch Hospital, New Zealand.
SOURCE: Arthritis and rheumatism, (1999 Mar) Vol. 42, No. 3, pp. 507-18.
Journal code: 0370605. ISSN: 0004-3591.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 20 Apr 1999
Last Updated on STN: 20 Apr 1999
Entered Medline: 5 Apr 1999

AB OBJECTIVE: To examine whether rheumatoid synovial fluid (SF) inhibits dendritic cell (DC) expression of the CD80 and CD86 costimulator molecules and contributes to SF T lymphocyte hyporesponsiveness. METHODS: Cell-free rheumatoid SF was tested for its effect on DC-stimulated autologous/allogeneic mixed lymphocyte reactions and for its effect on DC surface antigen expression, as assessed by flow cytometry. Blocking monoclonal antibodies were used to identify the SF cytokines that inhibited DC-T lymphocyte interactions. RESULTS: Low concentrations of SF (2.5%) could inhibit DC-mediated autologous and allogeneic T lymphocyte proliferation. This inhibitory effect could be reversed by neutralizing transforming growth factor beta (TGFbeta) and interleukin-2 (IL-2), but not by IL-12, in the SF. Hyaluronic acid, IL-6, IL-10, and tumor necrosis factor alpha were not associated with SF inhibition. In vitro culture alone and crosslinking with the

CD40 ligand up-regulated DC CD80/CD86 expression and costimulator function, and this was not affected by inclusion of SF. In the presence of SF, DC clustered with autologous T lymphocytes showed decreased CD80 and CD86 expression, and variable CD80/CD86 decreases were observed on DC clustered with allogeneic T lymphocytes. CONCLUSIONS: TGFbeta in SF appears to suppress T lymphocyte function, which may affect both signaling to DC and the induction of DC costimulator function.

L46 ANSWER 1 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2007:34276 CAPLUS
DOCUMENT NUMBER: 146:128639
TITLE: Drug-containing photocrosslinked hyaluronic acid derivative gel
INVENTOR(S): Miyamoto, Kenji; Yasuda, Yousuke
PATENT ASSIGNEE(S): Seikagaku Corporation, Japan
SOURCE: PCT Int. Appl., 46pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007004675	A1	20070111	WO 2006-JP313412	20060705

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: JP 2005-198176 A 20050706

AB Disclosed is a drug-containing photocrosslinked hyaluronic acid derivative gel which is a photocrosslinked hyaluronic acid gel containing a drug introduced through covalent bonding and has such properties that the gel can be pressed out from an injecting device. The drug-containing photocrosslinked hyaluronic acid derivative gel can be pressed out, for example, through a 20-25 gauge injection needle at a pressure of 0.5-5 kg/cm2. For example, aminopropyl naproxen ester hydrochloride was prepared, and reacted with aminopropyl cinnamate-modified sodium hyaluronate to obtain a white solid naproxen-introduced photoreactive hyaluronic acid derivative The obtained compound was filled in a glass syringe with a phosphate buffer, and light irradiated to form a gel of the present invention.

REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 2 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1304543 CAPLUS
DOCUMENT NUMBER: 146:50359
TITLE: Sustained-release anticancer agent sheets and their manufacture
INVENTOR(S): Nakayama, Yasuhide; Nemoto, Yasushi
PATENT ASSIGNEE(S): National Cardiovascular Center, Japan; Bridgestone Corp.
SOURCE: Jpn. Kokai Tokkyo Koho, 8pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2006335657	A	20061214	JP 2005-159377	20050531

PRIORITY APPLN. INFO.: JP 2005-159377 20050531

AB Aqueous solns. containing antitumor agents, hydrogen donors, and compds. selected from xanthene dye-modified collagen, fibronectin, gelatin, hyaluronic acid, keratan sulfate, chondroitin, chondroitin sulfate, elastin, heparan sulfate, laminin, thrombospondin, vitronectin, osteonectin, entactin, casein, polyethylene glycol, polypropylene glycol, polyglycidol, polyglycidol side-chain esterification products, poly(vinyl alc.), hydroxyethyl methacrylate-dimethylaminoethyl methacrylate copolymer, hydroxyethyl methacrylate-methacrylic acid copolymer, alginic acid, polyacrylamide, poly(dimethylacrylamide) and poly(vinylpyrrolidone) are spread on a surface and irradiated with visible light for photocrosslinking and insolubilization to give the sustained-release anticancer agent sheets. Approx. five eosin mols. were bound to amino groups of a gelatin mol. in the presence of a water-soluble carbodiimide to give eosin-modified gelatin. A solution containing the eosin-modified gelatin 10, 1,1,4,7,10,10-hexamethyltriethylenetetramine 1.2, and cytarabine (I) 1.0 weight% was applied on a sterilized dish and irradiated with visible light to give a .apprx.180 μm-thick red flexible sheet, which (50 mm + 50 mm) released approx. 5-20 mg/mL of I for .apprx.1 wk when immersed in 300 mL physiol. saline solution at 25°.

L46 ANSWER 3 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:1144617 CAPLUS
DOCUMENT NUMBER: 146:12988
TITLE: Antitumor sustained-release injection containing vascular inhibitor and cytotoxic drug
INVENTOR(S): Kong, Qingzhong; Yu, Jianjiang; Su, Hongqing
PATENT ASSIGNEE(S): Shandong Lan-Jin Bioengineering Co., Ltd., Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 30pp. CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1850049	A	20061025	CN 2006-10200542	20060609

PRIORITY APPLN. INFO.: CN 2006-10200542 20060609

AB The sustained-release injection is comprised of (A) sustained-release microsphere comprising effective constituent 0.5-60, sustained-release adjuvant 40-99% and suspending agent 0.0-30.0%; and (B) solvent. The antitumor effective constituent is selected from vascular inhibitor and/or and cytotoxic drug. Said vascular inhibitor is selected from gefitinib, tarceva, lapatinib, angiostatin, avastin, canertinib, panitumumab, etc., or the mixture thereof. Said cytotoxic drug is selected from one of camptothecin, procarbazine, taxol, cisplatin, carboplatin, chlorambucil, etc., or the mixture thereof. The sustained-release adjuvant is selected from one of (a) polylactic acid; (b) Polyglycolic acid-hydroxyacetic acid copolymer; (c) polifeprosan; (d) ethene-vinyl acetate copolymer; (e) difatty acid-sebacic acid copolymer; (f) poly(erucic acid dimer-sebacic acid) copolymer; (g) poly(fumaric acid-sebacic acid) copolymer; (h) sodium CM-cellulose, hydroxypropyl cellulose, xylitol, oligosaccharide, chondroitin, chitin, hyaluronic acid, collagens, etc.; or (i) racemic polylactic acid, etc., or the mixture thereof. The suspending agent is one of (a) 0.5-3.0 % (sodium) CM-cellulose; (b) 5-15 % mannitol; (c) 5-15 % sorbitol; (Crosslinked) 0.1-1.5 % surfactant; (e) 0.1-0.5 % tween 20; (f) (iodine) glycerin, dimethicone, propylene glycol, or carbomer; (g) 0.5-5 % sodium CM-cellulose + 0.1-0.5 % tween 80; (h) 5-20 % mannitol + 0.1-0.5 % tween 80; or (i) 0.5-5 % sodium CM-cellulose + 5-20 % sorbitol + 0.1-0.5 % tween 80. The product can inhibit tumor cell and blood vessel, also can increase local concentration and enhance

therapeutical effect.

L46 ANSWER 4 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2005:1177959 CAPLUS
DOCUMENT NUMBER: 143:446858
TITLE: Hyaluronic acid based copolymers
INVENTOR(S): Hossainy, Syed Faiyaz Ahmed; Michal, Eugene; Glauser, Thierry; Kwok, Connie; Pacetti, Stephen Dirk
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 11 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005244363	A1	20051103	US 2004-835912	20040430
WO 2005110505	A2	20051124	WO 2005-US14614	20050427
WO 2005110505	A3	20060706		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1750783	A2	20070214	EP 2005-743237	20050427
R: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LI, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR				

PRIORITY APPLN. INFO.: US 2004-835912 A 20040430
WO 2005-US14614 W 20050427

AB Hyaluronic acid (HA) conjugates or crosslinked HAs compns. for coating an implantable device are provided. The implantable device can be used for treating a disorder such as atherosclerosis, thrombosis, restenosis, high cholesterol, hemorrhage, vascular dissection or perforation, vascular aneurysm, vulnerable plaque, chronic total occlusion, claudication, anastomotic proliferation for vein and artificial grafts, bile duct obstruction, ureter obstruction, tumor obstruction, and combinations thereof.

L46 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:912280 CAPLUS
DOCUMENT NUMBER: 142:266540
TITLE: Anti-inflammatory drug delivery from hyaluronic acid hydrogels
AUTHOR(S): Hahn, Sei K.; Jelacic, Sandra; Maier, Ronald V.; Stayton, Patrick S.; Hoffman, Allan S.
CORPORATE SOURCE: Department of Bioengineering, University of Washington, Seattle, WA, 98195, USA
SOURCE: Journal of Biomaterials Science, Polymer Edition (2004), 15(9), 1111-1119
CODEN: JBSEEA; ISSN: 0920-5063
PUBLISHER: VSP BV
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two different types of hyaluronic acid (HA) hydrogels were synthesized by crosslinking HA with divinyl sulfone (DVS)

and poly(ethylene glycol)-divinyl sulfone (VS-PEG-VS). Vitamin E succinate (VES), an anti-inflammatory drug, and bovine serum albumin (BSA), a model of anti-inflammatory protein drugs, were loaded into the gels and their release kinetics were measured in vitro. VES and BSA released with a burst from both HA hydrogels during the first few hours, and release continued gradually for several days. The rate of release from HA-VS-PEG-VS-HA hydrogels was faster than that from HA-DVS-HA hydrogels, presumably due to the lower crosslink d. in the former. The anti-inflammatory action of released VES was tested by incubating peripheral blood mononuclear cells (PBMC) on HA hydrogels with and without VES in the gel. The number of cells adhering on HA hydrogels was very low compared to that on tissue culture polystyrene (TCPS), which might be one of the important advantages of using HA hydrogels for implant coatings or tissue engineering applications. ELISA test results showed that the tumor necrosis factor-α (TNF-α) concentration was very low in the supernatant of the wells containing the HA hydrogel with VES in contact with the activated macrophages compared to that without VES. This is probably the effect of the released VES reducing the production of anti-inflammatory cytokine, TNF-α. HA hydrogels containing anti-inflammatory drugs may have potential for use in tissue engineering and also as biocompatible coatings of implants.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L46 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:551368 CAPLUS
DOCUMENT NUMBER: 139:122818
TITLE: Biomaterials based on hyaluronic acid for the anti-angiogenic therapy in the treatment of tumors
INVENTOR(S): Fusenig, Norbert E.; Stark, Hans-Juergen; Willhauck, Michael; Pavesio, Alessandra
PATENT ASSIGNEE(S): Fidia Farmaceutici S.p.A., Italy; Deutsches Krebsforschungszentrum (DKFZ)
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003057203	A2	20030717	WO 2003-EP78		20030107
WO 2003057203	A3	20031231			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
IT 2002PD0003	A1	20030711	IT 2002-PD3		20020111
CA 2472880	A1	20030717	CA 2003-2472880		20030107
AU 2003201618	A1	20030724	AU 2003-201618		20030107
EP 1463541	A2	20041006	EP 2003-700315		20030107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
JP 2005524619	T	20050818	JP 2003-557561		20030107
US 2005037049	A1	20050217	US 2004-501030		20040812
PRIORITY APPLN. INFO.:			IT 2002-PD3	A	20020111
			WO 2003-EP78	W	20030107

AB The use in the medical-surgical field of biomaterials based on hyaluronic acid derivs., optionally in association with natural, synthetic or semi-synthetic biopolymers, for suppressing the angiogenic process associated with tumor proliferation (in primary and secondary tumors) is disclosed. For example, the Hyaff 11-based biomaterial proved able to modulate/inhibit the angiogenic process related to vascularization of the cancerous epithelium.

L46 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2003:9688 CAPLUS
DOCUMENT NUMBER: 139:138520
TITLE: Hyaluronan biomaterials for targeted drug delivery and wound healing
AUTHOR(S): Prestwich, Glenn D.; Luo, Yi; Kirker, Kelly R.; Ziebell, Michael R.; Shelby, Jane
CORPORATE SOURCE: Department of Medicinal Chemistry, The University of Utah, Salt Lake City, UT, 84112-5820, USA
SOURCE: Hyaluronan, [Proceedings of the International Cellucon Conference], 12th, Wrexham, United Kingdom, 2000 (2002), Meeting Date 2000, Volume 2, 277-284. Editor(s): Kennedy, John F. Woodhead Publishing Ltd.: Cambridge, UK.
CODEN: 69DKVZ; ISBN: 1-85573-570-9
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A mild chemical modification of hyaluronic acid (HA) provides functionalized derivs. for fabrication of targeted drug delivery systems, wound dressings, tissue engineering scaffolds, and probes for cellular binding and transport of HA. First, we describe the use of covalent HA-anti-cancer agents for use as potential therapeutics. Data from cell culture, flow cytometry, and in vivo mouse models support this targeted anti-tumor strategy. Second, we describe new flexible hydrogel films composed of crosslinked chondroitin sulfate (CS) and HA, which have potential as wound dressings capable of biointegration and drug release. Lyophilization and rehydration of these flexible films also provide porous materials for cell growth and tissue engineering. Third, we describe progress on the elucidation of the structure determination of the HA-binding domain (HABD) of RHAMM and the use of this domain to identify peptides that mimic HA.
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT